In the United States Court of Federal Claims

OFFICE OF SPECIAL MASTERS

Filed: May 29, 2024

JODY MADALA,	*	PUBLISHED
	*	
Petitioner,	*	No. 19-1182V
	*	
v.	*	Special Master Dorsey
	*	
SECRETARY OF HEALTH AND HUMAN SERVICES,	*	Dismissal; Influenza ("Flu") Vaccine; Goodpasture's Syndrome; Anti-GBM Disease.
	*	
Respondent.	*	
	*	

Heather Marie Schneider, The Locks Law Firm, Philadelphia, PA, for Petitioner.
Tyler King, U.S. Department of Justice, Washington, DC, for Respondent.

DECISION[1]

On August 13, 2019, Jody Madala ("Petitioner") filed a petition for compensation under the National Vaccine Injury Compensation Program ("Vaccine Act" or "the Program"), 42 U.S.C. § 300aa-10 et seq. (2018),[2] alleging that she suffered from acute renal failure and/or Goodpasture's syndrome as a result of receiving an influenza ("flu") vaccination on October 11, 2016. Petition at Preamble (ECF No. 1). Respondent argued against compensation, stating the

[1] Because this Decision contains a reasoned explanation for the action in this case, the undersigned is required to post it on the United States Court of Federal Claims' website and/or at https://www.govinfo.gov/app/collection/uscourts/national/cofc in accordance with the E-Government Act of 2002. 44 U.S.C. § 3501 note (2018) (Federal Management and Promotion of Electronic Government Services). **This means the Decision will be available to anyone with access to the Internet.** In accordance with Vaccine Rule 18(b), Petitioner has 14 days to identify and move to redact medical or other information, the disclosure of which would constitute an unwarranted invasion of privacy. If, upon review, the undersigned agrees that the identified material fits within this definition, the undersigned will redact such material from public access.

[2] The National Vaccine Injury Compensation Program is set forth in Part 2 of the National Childhood Vaccine Injury Act of 1986, Pub. L. No. 99-660, 100 Stat. 3755, codified as amended, 42 U.S.C. §§ 300aa-10 to -34 (2018) ("Vaccine Act" or "the Act"). All citations in this Decision to individual sections of the Vaccine Act are to 42 U.S.C.A. § 300aa.

case was "not appropriate for compensation under the terms of the Act." Respondent's Report ("Resp. Rept.") at 1 (ECF No. 30).

After carefully analyzing and weighing the evidence presented in accordance with the applicable legal standards, the undersigned finds Petitioner has failed to provide preponderant evidence that the flu vaccination caused her to develop acute renal failure and/or Goodpasture's syndrome. Thus, Petitioner has failed to satisfy her burden of proof under Althen v. Secretary of Health & Human Services, 418 F.3d 1274, 1280 (Fed. Cir. 2005). Accordingly, the petition must be dismissed.

I. ISSUES TO BE DECIDED

Diagnosis is not at issue. The parties agree that Petitioner suffers from anti-glomerular basement membrane ("anti-GBM") disease/Goodpasture's syndrome. Joint Submission, filed June 15, 2023, at 1 (ECF No. 106). However, the parties dispute onset of Petitioner's condition. Id. They also dispute causation and whether Petitioner has provided preponderant evidence for all three Althen prongs. Id.

II. BACKGROUND

A. Medical Terminology

Goodpasture's syndrome is an "inflammatory pulmonary-renal syndrome that largely affects the glomerular capillaries in the kidney and alveolar capillaries in the lung." Resp. Exhibit ("Ex.") D at 3. It is a "rare [] organ-specific autoimmune disease . . . [that] typically presents as acute renal failure caused by a rapidly progressive glomerulonephritis."[3] Resp. Ex. D, Tab 3 at 1.[4] Although great progress has been made in understanding its pathogenesis, the etiology of the illness remains unknown. Id.

Symptoms may begin slowly or rapidly, "gradually affecting the lungs and [] kidneys. . . . Initial symptoms may include fatigue, weakness, [] nausea and/or vomiting, loss of appetite, [and] unhealthy, pale appearance." Resp. Ex. D, Tab 3 at 2. These symptoms may "precede or be concurrent with pulmonary or renal manifestations." Id. "If the disease affects the kidneys, it

[3] Glomerulonephritis is a "nephritis accompanied by inflammation of the capillary loops in the renal glomeruli. It occurs in acute, subacute, and chronic forms and may be secondary to hemolytic streptococcal infection. Evidence also supports possible immune or autoimmune mechanisms." Glomerulonephritis, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=20383 (last visited Apr. 15, 2024). Nephritis is "inflammation of the kidney." Nephritis, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=33488 (last visited Apr. 15, 2024).

[4] Antonio Greco et al., Goodpasture's Syndrome: A Clinical Update, 14 Autoimmunity Revs. 246 (2015).

may cause . . . hematuria [blood in the urine]." Id. "Other renal manifestations include edema and eventually uremia."[5] Id.

Diagnosis is confirmed by the presence of anti-GBM antibodies. Resp. Ex. D, Tab 3 at 2, 4. For this reason, Goodpasture's syndrome is also referred to as "anti-GBM disease." Id. at 2. Anti-GBM disease is "characterized by autoantibodies directed against the glomerular[] basement membrane"[6] in the kidneys and the alveolar basement membrane in the lungs. Id. Some patients with anti-GBM/Goodpasture's disease have antineutrophil cytoplasmic antibodies ("ANCAs")[7] as well as anti-GBM antibodies.[8] Id. at 4. These patients are referred to as "double-positive" or double seropositive. Id. Double-positive patients have different histology

[5] Uremia refers to "the entire constellation of signs and symptoms of chronic renal failure, including nausea, vomiting, anorexia, a metallic taste in the mouth, a characteristic odor of the breath, pruritus, urea frost on the skin, neuromuscular disorders, pain and twitching in the muscles, hypertension, edema, mental confusion, and acid-base and electrolyte imbalances." Uremia, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=51984 (last visited May 8, 2024).

[6] The glomerular basement membrane, or GBM, "serves as the skeleton of the glomerular tuft. . . . The major components of the [GBM] are laminin and type IV collagen." Thomas J. Guzzo & Drew A. Torigain, Kidney and Ureter, in Grey's Anatomy: The Anatomical Basis of Clinical Practice 1237, 1248 (Susan Standring et al. eds., 41st ed. 2016). Collagen refers to "any of a family of extracellular, closely related proteins occurring as a major component of connective tissue, giving it strength and flexibility." Collagen, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=10488 (last visited May 15, 2024). The Collagen IV family forms complex chain networks in the GBM playing a crucial role in tissue function and cell receptor interactions. Pet. Ex. 22 at 2 (Stephen P. McAdoo & Charles D. Pusey, Anti-Glomerular Basement Membrane Disease, 12 Clinical J. Am. Soc'y Nephrology 1162 (2017)); Resp. Ex. B, Tab 4 at 1, 7-9 (Billy G. Hudson, The Molecular Basis of Goodpasture and Alport Syndromes: Beacons for the Discovery of the Collagen IV Family, 15 J. Am. Soc'y Nephrology 2514 (2004)).

[7] ANCA is "an autoantibody to cytoplasmic constituents of monocytes and neutrophils, found in increased amounts in some types of vasculitis." Antineutrophil Cytoplasmic Autoantibody, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=59689 (last visited Apr. 15, 2024). Vasculitis is the "inflammation of a blood or lymph vessel." Vasculitis, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=52617 (last visited May 15, 2024).

[8] But see Resp. Ex. D, Tab 1 at 1 ("The term Goodpasture's syndrome should be reserved for patients with pulmonary-renal vasculitis syndrome caused by anti-GBM antibodies," not when the syndrome is caused by ANCA-pulmonary capillaries.) (J.C. Jennette & D.B. Thomas, Crescentic Glomerulonephritis, 16 Nephrology Dialysis Transplant 80 (2001)). For the purpose of this Decision, the undersigned will use the phrase anti-GBM disease or anti-GBM/Goodpasture's syndrome to specify Petitioner's illness, which is distinct from ANCA-associated diseases.

findings as compared to patients who have only anti-GBM antibodies. Id. at 4, 5. "Aggressive therapy with plasmapheresis, corticosteroids, and immunosuppressive agents has dramatically improved prognosis" in anti-GBM/Goodpasture's disease. Id. at 5. With appropriate treatment, the majority of patients do not require long-term dialysis. Id.

B. Procedural History

Petitioner filed her petition on August 13, 2019. Petition. Petitioner filed affidavits and medical records on September 3, 2019.[9] Pet. Exs. 1-12. Respondent filed his Rule 4(c) report, arguing against compensation, on September 16, 2020. Resp. Rept. at 1.

Petitioner filed expert reports from Dr. Carl S. Goldstein and Dr. Gourang P. Patel on January 15, 2021. Pet. Exs. 16-17. Respondent filed expert reports from Dr. George Jarad and Dr. Arnold Levinson on December 1, 2021. Resp. Exs. B, D. Petitioner filed a supplemental expert report from Dr. Goldstein on January 18, 2022. Pet. Ex. 45.

A Rule 5 conference was held on February 1, 2022. Rule 5 Order dated Feb. 1, 2022 (ECF No. 76). The undersigned was unable to provide her preliminary opinion as to onset and indicated additional expert reports regarding onset would be helpful. Id. at 1. The undersigned found Petitioner's theory was underdeveloped and explained that an expert report from an immunologist would also be helpful. Id. at 1-2. Petitioner was ordered to file an expert report from an immunologist in sixty days. Id.

After multiple motions for extension of time to file an expert report from an immunologist, Petitioner filed a status report indicating she was unable to comply with the Court's order. Pet. Status Rept., filed Dec. 2, 2022 (ECF No. 90). Petitioner reported she had previously retained an expert in immunology, but "due to the rarity/novel nature of Petitioner's injury, the immunologic expert retained . . . ultimately concluded they were unable to write a report." Id. at 1. "Petitioner contacted numerous qualified experts in immunology in an exhaustive search, including Petitioner's treating physicians," but Petitioner was "unable to secure a qualified immunologist to write an expert report." Id. at 2.

On January 17, 2023, Petitioner filed a joint status report indicating that although she was unable to retain an expert in immunology, her position on the etiology of Petitioner's injury remained unchanged. Pet. Joint Status Rept., filed Jan. 17, 2023 (ECF No. 93). The parties requested a status conference to discuss the next steps. Id. at 1. At a status conference on February 2, 2023, Respondent indicated he was not interested in settlement. Order dated Feb. 2, 2023 (ECF No. 94). Petitioner indicated she wanted to file a supplemental expert report from Dr. Goldstein. Id. at 1.

On March 15, 2023, Petitioner filed a joint status report indicating that because Dr. Goldstein previously filed a supplemental expert report in response to Respondent's experts, Petitioner no longer wished to provide an additional expert report. Pet. Joint Status Rept., filed

[9] Petitioner continued to file medical records throughout the course of litigation.

Mar. 15, 2023 (ECF No. 96). The parties also indicated they agreed to resolve entitlement through a ruling on the record. Id. at 1.

Petitioner filed a motion for a ruling on the record on May 31, 2023. Pet. Motion for Ruling on the Record ("Pet. Mot."), filed May 31, 2023 (ECF No. 101). Respondent filed his response on September 19, 2023. Resp. Response to Pet. Mot. ("Resp. Response"), filed Sept. 19, 2023 (ECF No. 111). Petitioner did not file a reply.

This matter is now ripe for adjudication.

C. Factual History

1. Summary of Medical Records

a. Pre-Vaccination

Prior to the vaccination at issue, Petitioner had a history of hypothyroidism and ovarian cysts. Pet. Ex. 10 at 16; Pet. Ex. 13 at 67.

Petitioner visited Presbyterian Hospital on June 10, 2016 for pharyngitis and reported bumps on the back of her throat since the prior Friday. Pet. Ex. 51 at 1-2. History of present illness indicated Petitioner had experienced "a little discomfort," but was feeling better, had no fever, and had some change in her sense of taste. Id. at 12. Petitioner reported alcohol intake as one drink per week. Id. at 13. Other than levothyroxine for her thyroid condition and Necon (birth control), she was not taking any other medication. Id. She had no other reported symptoms and was diagnosed with "mild hypertrophy[10] of [tongue] papillae"[11] and instructed to continue gargling with Listerine. Id. at 14.

On June 27, 2016, Petitioner returned to Presbyterian Hospital, complaining of "shaking in [her] hands" the prior Saturday "for about 10 minutes." Pet. Ex. 51 at 32. She also reported that she had a "drooping left eyelid [for one] year." Id. At the visit she was noted to be afebrile. Id. at 34. Blood work, including a complete blood count ("CBC"), creatinine,[12] and iStat 6, was

[10] Hypertrophy is "the enlargement or overgrowth of an organ or part due to an increase in size of its constituent cells." Hypertrophy, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=24054 (last visited May 9, 2024).

[11] Papillae of the tongue are "threadlike elevations that cover most of the tongue surface." Papillae Filiformes, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=95936 (last visited May 9, 2024).

[12] Creatinine is "the cyclic anhydride of creatine" excreted in the urine and measurements of excretion rates are used as diagnostic indicators of kidney function." Creatinine, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=11586 (last visited Apr. 15, 2024).

collected. Id. at 37. Her CBC, thyroid stimulating hormone, and creatinine were normal.[13] Id. at 38-42. Her iStat 6 results were all normal except her chloride, which was elevated at 111 (reference range 98-109 mmol/L). Id. at 39-40, 42. Petitioner was diagnosed with a "[t]remor of uncertain etiology [] possibly due to hypoglycemic episode in that it seemed to resolve after eating." Id. at 42. Her drooping left eyelid was attributed to swelling from allergies. Id.

It appears Petitioner also had kidney stones prior to her vaccination, but no documentation of related medical visits or treatment was provided. See Pet. Ex. 3 at 21 (indicating "[history] of kidney stones and ovarian cysts" at an October 21, 2016 urgent care visit); Pet. Ex. 5 at 2 (noting kidney stones in Petitioner's past history at an emergency department ("ED") visit on October 21, 2016); Pet. Ex. 7 at 33 (nephrologist stating Petitioner "denied any history of chronic kidney disease" and noted "[s]he had kidney stones in the past two months" at a consultation on October 27, 2016).[14]

Petitioner received the Flulaval Quadrivalent flu vaccine in her right deltoid on October 11, 2016. Pet. Ex. 2 at 1-2.

b. Post-Vaccination

On October 21, 2016, Petitioner presented to Presbyterian urgent care complaining of blood in her urine (hematuria) that started the night before. Pet. Ex. 3 at 13. She also complained of one episode of vomiting and decreased appetite, "start[ing] almost two weeks ago after getting the flu shot." Id. at 13, 16. Petitioner reported the three nights following her flu shot, she woke up sweating. Id. She reported a headache but thought it could be due to not eating. Id. Petitioner also reported chest pain, chills, a mild cough, nasal congestion, shortness of breath, myalgias, and chest pressure with deep breaths, for two weeks. Id.

Physical examination was normal, except for tenderness in the lower sternal area and mild tenderness in the epigastric area. Pet. Ex. 3 at 14. Lab testing revealed large amount of blood in her urine (hematuria) and elevated creatinine of 2.6 (reference range 0.6-1.0 mg/dL). Id. at 14-16. White blood cell ("WBC") count was elevated at 12.2 (reference range 4.0-11.0); sodium was abnormally low at 133 (reference range 138-146 mmoL/L); red blood cell count, hemoglobin, hematocrit, platelet counts, and absolute neutrophils were also all abnormal. Id. Rapid strep A testing was normal. Id. at 15. Petitioner stated that she had been taking over the counter ibuprofen for her headache. Id. at 16. She also reported a history of kidney stones. Id. Dr. Jeanelle O'Kious referred her to the ED due to her elevated creatinine "which could indicate acute kidney damage." Id.

[13] On June 27, 2016, iStat creatinine was 0.8 (reference range 0.6-1.0 mg/dL).

[14] In her affidavit, executed August 13, 2019, Petitioner attested that prior to the vaccination at issue, she "did not have any signs, symptoms, or diagnosis of any renal disease or kidney disorders." Pet. Ex. 1 at 2. This was affirmed in Petitioner's motion for a ruling on the record. Pet. Mot. at 1.

Petitioner presented to Christus St. Vincent's Regional Medical Center ("Christus Hospital") ED on October 21, 2016. Pet. Ex. 5 at 2. Chief complaint was high creatinine level and blood in urine. Id. Petitioner reported "she got the flu shot [two] weeks ago and . . . had [symptoms] since then." Id. Petitioner took 800 mg of ibuprofen four times per day for the past two weeks. Id. She stopped taking ibuprofen two days prior to this visit. Id. Repeat labs showed her creatinine was 2.2 mg/dL. Id. at 4, 26. Review of systems was positive for sweating, nausea, constipation, decreased appetite, and headache. Id. at 2. Past history included kidney stones. Id. Physical examination was unremarkable, but a renal ultrasound showed "[m]ildly echogenic kidneys" suggestive of "medical renal disease." Id. at 2-3, 55. Dr. Eric Robert Ladd noted that there was "likely [a] pre-renal cause, although ibuprofen [was a] possible cause." Id. at 3. The diagnosis was acute kidney injury and hematuria. Id. at 4. She was discharged and instructed to have lab work repeated and to consult with nephrology. Id. at 3.

Repeat labs done on October 24, 2016 revealed Petitioner's creatinine was even more elevated at 5.84 mg/dL. Pet. Ex. 6 at 4. ANCA was negative. Id. On October 25, 2016, Petitioner saw nephrologist Dr. Alexandra Voinescu for "evaluation and treatment of sudden onset of macroscopic hematuria and acute kidney injury." Id. at 1. Petitioner "reported getting sick approximately two weeks ago after receiving the flu vaccine with symptoms of headache, muscle aches, cough, fatigue[,] and night sweats," for which she started taking ibuprofen four to five times daily. Id. "She presented to [urgent care] on Friday for new onset gross hematuria associated with persistent malaise, poor appetite[,] and nausea. Routine blood work showed creatinine level of 2.6 mg/dL (from baseline creatinine level 0.8 mg/dL)." Id. "She was subsequently sent to the [ED] where repeat creatinine level was found to be 2.2 mg/dL. The patient was instructed to stop all [non-steroidal anti-inflammatory drugs ("NSAIDs")] and was referred . . . for further evaluation." Id. Petitioner did not report any history of "throat/sinus infections, no rashes, no photosensitivity, no autoimmune diseases, and no [family history] of hematuria/kidney disease." Id.

Renal risk assessment included the use of NSAIDS, noting the use of "[i]buprofen in the last [two] weeks." Pet. Ex. 6 at 1. Petitioner reported that she was "a social drinker." Id. at 2. Dr. Voinescu's assessment was "[a]cute kidney injury with nephritic syndrome, likely glomerular etiology (such as [immunoglobulin ("Ig")] A nephropathy[15] vs. other

[15] IgA nephropathy is "a common, chronic form of glomerulonephritis marked by hematuria and proteinuria and by deposits of immunoglobulin A in the mesangial areas of the renal glomeruli, with subsequent reactive hyperplasia of mesangial cells." IgA Nephropathy, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=91761 (last visited Apr. 15, 2024). Mesangial cells are "phagocytic cells found in the mesangium of the glomerulus of the kidney, thought to aid in cleaning the filtration apparatus." Mesangial Cells, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=64250 (last visited May 8, 2024).

glomerulonephritis) vs. NSAIDs-induced [acute interstitial nephritis ("AIN")]."[16] Id. at 5. Serology testing was ordered. Id. The plan was to admit Petitioner to the hospital for a renal biopsy. Id.

Petitioner was hospitalized at Christus Hospital from October 25 to October 27, 2016. Pet. Ex. 5 at 76, 78. Intake notes indicated Petitioner had no significant medical history but "began feeling generally unwell around mid October. She developed upper respiratory tract symptoms and went to [] urgent care" where her creatinine was noted to be elevated. "There was no obvious etiology for this increase in creatinine." Id. at 74. Petitioner reported feeling "generally weak" and nauseated. Id. Assessment was acute rental failure. Id. at 76. It was noted that Petitioner had "been using nonsteroidal anti-inflammatory drugs recently, which [was] a possibility." Id.

Progress notes from October 26 stated Petitioner "had an [upper respiratory infection ("URI")] several weeks ago and [] had progressively worsening renal failure since." Pet. Ex. 5 at 109. "Creatinine had increased from baseline 0.6 to 8.3 in a few weeks, may be related to preceding URI, associated with anemia and hematuria, autoimmune studies neg[ative], unremarkable renal [ultrasound]." Id. at 76, 78, 110, 126. A left renal biopsy performed on October 26 revealed "anti-[GBM] associated severe necrotizing and crescentic glomerulonephritis, diffuse," and "diffuse and severe" "acute tubular injury." Pet. Ex. 6 at 7. A chest X-ray was normal and did not show any pulmonary infiltrates. Pet. Ex. 5 at 276. Petitioner was started on intravenous ("IV") corticosteroids (Solumedrol). Id. at 78, 102. On October 27, Petitioner's creatinine was 10.7 mg/dL. Id. at 83. Petitioner requested a transfer to Presbyterian Hospital in Albuquerque, and she was discharged from Christus Hospital on October 27. Id. at 78. Primary discharge diagnosis was "[a]cute renal failure with nephritic syndrome – secondary to [rapidly progressive glomerulonephritis ("RPGN")[17]] with positive [anti-GBM] antibody." Id. at 78, 86, 92.

[16] AIN is "a type of interstitial nephritis usually seen as a complication of a systemic infection, especially by beta-hemolytic streptococci, although it sometimes has an allergic etiology. . . . It often resolves if the infection is treated, or the offending drug or allergen is removed." Acute Interstitial Nephritis, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=91682 (last visited Apr. 15, 2024). Interstitial nephritis is a "primary or secondary disease of the renal interstitial tissue. Causes include arterial, arteriolar, glomerular, or tubular disease that destroys individual nephrons; toxic involvement of interstitial cells and tubules" by systemic diseases, drug exposure, and mercury poisoning. Interstitial Nephritis, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=91703 (last visited Apr. 15, 2024).

[17] RPGN is an "acute glomerulonephritis marked by a rapid progression to end-stage renal disease and, histologically, by profuse epithelial proliferation, often with epithelial crescents; principal signs are anuria, proteinuria, hematuria, and anemia." Rapidly Progressive Glomerulonephritis, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=79030 (last visited Apr. 15, 2024).

Petitioner was hospitalized at Presbyterian Hospital from October 27 to November 28, 2016 for management of her condition. Pet. Ex. 7 at 10. Admission notes indicated Petitioner "had URI with hematuria mid-October," presented to urgent care with elevated creatinine, referred to nephrologist, admitted to Christus Hospital for kidney biopsy, and subsequently transferred Presbyterian Hospital. Id. at 16, 20. It was noted that Petitioner's "kidney function ha[d] continued to decline . . . as she [was] in worsening renal failure." Id. In a nephrology consultation on October 27, Dr. Thelmo Barrantes-Ramirez noted Petitioner "developed an acute respiratory illness after a flu vaccine about [two] weeks ago. She developed chills initially with significant use of NSAIDS temporarily." Id. at 33. He added Petitioner had a kidney biopsy the day before "that showed anti-GBM disease with minimal interstitial fibrosis of chronic changes" and that her creatinine rose from 2.2 to 13 in one week. Id. Her anti-GBM titer was 550 (normal range 0-19 AU/mL). Id. at 34. At Petitioner's first infusion center consultation, Dr. Benjamin Wagenman wrote Petitioner "began feeling ill shortly after receiving a[] [flu] vaccine on [October 11, 2016] . . . . [s]he started having chills, nausea, and headaches[,] . . . and later developed pain with urination and hematuria." Id. at 35. After her initial visit to the ED on October 21, "she continued to feel worse." Id. at 36. His assessment was acute RPGN with anti-GBM antibody pattern confirmed on renal biopsy[18] and Petitioner was "in need of emergent therapeutic plasma exchange."[19] Id. at 37.

During hospitalization at Presbyterian Hospital, Petitioner was treated with hemodialysis,[20] corticosteroids, cyclophosphamide,[21] plasmapheresis,[22] and mycophenolate

[18] Dr. Wagenman noted there was no evidence of pulmonary involvement at that time. Pet. Ex. 7 at 37.

[19] Dr. Wagenman opined that with Petitioner's "creatinine as high as it [was], there [was] no guarantee that she [would] recover her renal function, but . . . it [was] worth trying, especially since the rapid increase seem[ed] to have occurred just in the past week." Pet. Ex. 7 at 38.

[20] Hemodialysis is "the removal of certain elements from the blood by virtue of the difference in the rates of their diffusion through a semipermeable membrane. Two distinct physical processes are involved, diffusion and ultrafiltration." Hemodialysis, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=22016 (last visited Apr. 15, 2024).

[21] Cyclophosphamide is "a cytotoxic alkylating agent of the nitrogen mustard group, used as an antineoplastic, often in combination with other agents, for a wide variety of conditions; . . . also used as an immunosuppressive agent to prevent transplant rejection and in the treatment of certain diseases with abnormal immune function." Cyclophosphamide, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=12166 (last visited Apr. 15, 2024).

[22] Plasmapheresis is "the removal of plasma from withdrawn blood, with retransfusion of the formed elements into the donor; generally, type-specific fresh frozen plasma or albumin is used to replace the withdrawn plasma." Plasmapheresis, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=39455 (last visited Apr. 15, 2024).

mofetil.[23] Pet. Ex. 7 at 11-12, 184-85. She had a renal ultrasound that showed nonspecific findings, but it was noted that "in this patient [,] [the findings were] likely related to either chronic medical renal disease or underlying glomerulonephritis." Id. at 10, 184. Additionally, chest X-rays revealed "moderate vascular congestion with bibasilar pleural effusion." Id. at 10-11. Her hospital course was complicated with anemia of acute inflammation and hypertension associated with renal disorder. Id. at 200. Petitioner's discharge diagnosis was "RPGM (Goodpasture's)." Id. at 12, 184-85. It was noted that Petitioner's "biopsy results were positive for this." Id. at 12. At time of discharge Petitioner's creatinine was 7.62 mg/DL and her anti-GBM titer was 23 AU/mL (the goal for discharge was below 30 AU/mL). Id. at 12, 184-85, 188. The plan was to continue medications and hemodialysis as an outpatient. Id. at 12.

Following discharge on November 28, 2016, Petitioner continued hemodialysis as an outpatient with Home Dialysis of New Mexico overseen by Dr. Sonam Kundeling. Pet. Ex. 7 at 11-12; Pet. Ex. 8 at 6. Petitioner had dialysis three days per week until January 2, 2017, then switched to two days per week until January 20, 2017.[24] Pet. Ex. 8 at 6-7, 9-10, 37, 169. Throughout this time, Petitioner's creatinine and anti-GBM titer decreased. Id. at 53, 51-98, 107-09. Her last creatinine measured during this time was 3.12 mg/dL, and her last anti-GBM titer was 13 AU/mL. Id. at 51, 71.

On March 16, 2017, Petitioner visited Dr. Ranil DeSilva, a nephrologist in Pittsburgh, Pennsylvania, to get a second opinion regarding her anti-GBM related kidney disease and to establish care in Pittsburgh in advance of an upcoming move from New Mexico to Pennsylvania. Pet. Ex. 12 at 483. Petitioner reported that on October 11, 2016, she received a flu vaccine and "within 24 h[ours] felt myalgias/chills/night sweats." Id. At the time of this visit, Petitioner was only taking prednisone. Id. at 484. Dr. DeSilva noted that Petitioner continued to have "mild active sediment" and recommended monthly anti-GBM checks and continued steroid use with a slow taper. Id. at 487. She was then evaluated on April 4, 2017, by Dr. Mona Anand, an internist in Pittsburgh, as part of an evaluation for a potential renal transplant. Pet. Ex. 13 at 5.

By June 2017, Petitioner had moved to Pittsburgh. Pet. Ex. 12 at 395. On June 6, 2017, Dr. DeSilva observed that the sediment findings in Petitioner's urine had improved and advised a continued tapering of her steroids. Id. at 398, 432. At an October 10, 2017, visit with Dr. DeSilva, Petitioner was "doing well" and her anti-GBM titers were negative. Id. at 335, 337. She was advised to discontinue the prednisone completely, follow-up with the transplant service, and stop anti-GBM monitoring. Id. at 338.

Petitioner continued to see Dr. DeSilva and Dr. Anand on a regular basis. See Pet. Exs. 12-13. In September 2018, Petitioner's renal function was determined to be "stable," and

[23] Mycophenolate mofetil is "an immunosuppressive agent used in conjunction with cyclosporine and corticosteroids to prevent rejection of allogeneic renal, hepatic, and cardiac transplants." Mycophenolate Mofetil, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=32633 (last visited Apr. 15, 2024).

[24] Petitioner was officially discharged from Home Dialysis of New Mexico on February 8, 2017. Pet. Ex. 8 at 109.

Petitioner was not requiring dialysis but remained on the transplant list. Pet. Ex. 13 at 56-57. In 2019, Petitioner sought a second opinion at the Mayo Clinic with nephrologist Dr. John Dillon regarding evaluation for a kidney transplant. See Pet. Ex. 50. To date, it does not appear Petitioner has received a kidney transplant.

No other relevant medical records were filed.

2. Affidavits

a. Petitioner[25]

Prior to the vaccination at issue, Petitioner was the chief executive officer ("CEO") of Madala Health, her own healthcare consulting firm headquartered in New Mexico. Pet. Ex. 1 at 2. Her past medical history included hypothyroidism and an ovarian cyst, which were both controlled by medication. Id. Petitioner explained that prior to the vaccination at issue, she "did not have signs, symptoms, or diagnosis of any renal disease or kidney disorders." Id.

While visiting her parents in New Jersey, Petitioner received a flu vaccine on October 11, 2016. Pet. Ex. 1 at 2. "Within 24 hours, [Petitioner] began to feel malaise, cold chills, and experience[d] night sweats." Id. at 3. Approximately one week after vaccination, Petitioner had "nausea/vomiting, loss of appetite[,] and blood in the urine." Id. During this time, Petitioner returned to her home in New Mexico. Id.

On October 21, 2016, "after experiencing the aforementioned symptoms for ten days," Petitioner presented to urgent care where she saw Dr. O'Kaus. Pet. Ex. 1 at 3. A urinalysis revealed elevated creatinine levels and Petitioner was referred to the ED. Id. Dr. Ladd examined Petitioner at the ED where he instructed Petitioner to rest and increase her fluid intake. Id. Labs were ordered and she was discharged. Id.

Petitioner presented to the Nephrology Renal Clinic for the recommended bloodwork on October 24, 2016. Pet. Ex. 1 at 3. Dr. Voinescu reviewed the blood test results and diagnosed Petitioner with "acute kidney injury with nephritic syndrome." Id. at 3-4. Dr. Voinescu also recommended a renal biopsy. Id. That same day, Petitioner was admitted to Christus Hospital with "sudden acute renal failure and immediate need for a kidney biopsy." Id. at 4. On October 27, while hospitalized, Petitioner received a diagnosis of "IgG Glomerulonephritis, which was later confirmed to be Goodpasture [syndrome] after the return of the kidney biopsy." Id.

Petitioner was transferred to Presbyterian Hospital where she remained for inpatient treatment related to acute kidney failure and Goodpasture's syndrome for 31 days until her discharge on November 28, 2016. Pet. Ex. 1 at 4. Her diagnosis at the time of discharge was acute kidney injury, acute renal failure, and RPGN. Id.

Following discharge from the hospital, Petitioner's treating physicians ordered her to receive in-home dialysis three time per week. Pet. Ex. 1 at 4. By January 2017, Petitioner's

[25] Petitioner also provided a diary describing her course in much more detail. See Pet. Ex. 4.

creatinine levels began to stabilize, and her home dialysis was reduced to two times per week and "to be tapered off completely until a future date when [Petitioner would require a kidney transplant." Id.

On December 14, 2016, Petitioner filed a VAERS report. Pet. Ex. 1 at 4. Petitioner maintained "the renal failure caused by the [flu] vaccine . . . was the 'cause-in-fact' of [her] acute kidney failure, Goodpasture['s] syndrome, and low remaining kidney function that will ultimately require an invasive kidney transplant." Id. at 4-5.

b. Petitioner's Parents

Das B. Madala and Nirmaladas Madala are Petitioner's parents. Pet. Ex. 1 at 6. They explained Petitioner was in Pittsburgh for work on October 7, 2016, and her parents joined her on October 9, 2016 for Petitioner's birthday. Id. On October 10, the three of them drove back to Petitioner's parents' home in New Jersey. Id. Petitioner stayed with her parents from October 10 to October 18, 2016. Id. While there, Petitioner received the flu vaccination on October 11. Id.

Within 24 hours of Petitioner receiving her vaccination, her parents observed that Petitioner "began to feel malaise, cold chills, and experience[d] night sweats." Pet. Ex. 1 at 7. The morning of October 12, 2016, Petitioner informed her parents that "she had experienced severe night sweats the night before and had to change her pajamas during the night because they had become drenched with sweat." Id. They stated Petitioner did not experience these symptoms in the nights before while she was staying with them. Id. Her parents recalled Petitioner was "unenthusiastic and unmotivated showing low energy levels that are not normal of her typical behavior." Id. "Even in her worst state, she still tried to go meet a friend at [their] local diner on October 14, 2016, but could only stay for a brief period of time. She returned home very quickly which is very unlike her." Id. Petitioner's parents "assumed [Petitioner's] symptoms were expected and would subside as she developed immunity to the flu in a week or two. With that in mind, [they] did not take her to see a healthcare provider to seek treatment," which they "regret [] very much." Id.

Petitioner continued to experience these symptoms for the duration of her stay with her parents and the "symptoms continued to worsen over those days." Pet. Ex. 1 at 7. Petitioner's parents recalled Petitioner began to have trouble eating. She had no appetite at all and slept much of the day. Id. Petitioner left her parents' house to go back to New Mexico on October 18, 2016. Id.

On October 20, 2016, Petitioner's parents travelled to New Mexico to visit Petitioner for a previously planned vacation. Pet. Ex. 1 at 7. Petitioner picked them up from the airport and informed them she was "still experiencing the same aforementioned symptoms since the flu shot, and that her condition had not improved and even felt worse." Id. at 7-8. When they arrived back to Petitioner's house from the airport, Petitioner went to the restroom, "and upon leaving the restroom informed [her parents] that she had noticed that there was blood in her urine." Id. at 8. They all agreed should seek medical treatment as soon as possible. Id. Because it was

already late in the evening, Petitioner waited until the next morning, October 21, to go to urgent care. Id.

Petitioner was subsequently hospitalized for 30 days. Pet. Ex. 1 at 8. Petitioner's parents postponed their flights home and stayed in New Mexico to provide any support they could. Id. They were "present for every treatment and medication [Petitioner] received for several months after her end of November discharge." Id.

D. Expert Reports

1. Petitioner's Expert, Dr. Carl S. Goldstein, M.D.[26]

a. Background and Qualifications

Dr. Goldstein is a board-certified nephrologist. Pet. Ex. 30 at 4. He received his M.D. from Washington University in St. Louis, Missouri. Id. at 2. Thereafter, he completed an internship and residency at the University of Minnesota, and nephrology fellowships at the Hospital of the University of Pennsylvania. Id. He is currently the Division Chief of Nephrology and Director of Dialysis Services at Overlook Medical Center in Summit, New Jersey. Id. He is also a Clinical Professor of Medicine at Rutgers University. Id. at 4. Dr. Goldstein has authored or co-authored numerous publications. Id. at 6-8.

b. Opinion

Dr. Goldstein opined it is "reasonable and probable to conclude that the induction of Goodpasture's disease, an autoimmune phenomenon, is consequent to and the result of [the flu] vaccination in this case." Pet. Ex. 16 at 2.

i. Althen Prong One

Dr. Goldstein opined that the mechanism of injury here "is unknown but clearly different from other accepted triggers of anti-GBM disease." Pet. Ex. 45 at 2. He explained that Goodpasture's syndrome is a rare disease and significant adverse events to flu vaccination are similarly rare. Id. at 1-2. "At the intersection of two rare clinical events is always some mechanistic uncertainty." Id. at 2. Dr. Goldstein agreed that the Institute of Medicine ("IOM") found "[t]he evidence [was] inadequate to accept or reject a causal relationship between the [flu] vaccine and vasculitis." Pet. Ex. 16 at 5 (quoting Pet. Ex. 32 at 92).[27] But Dr. Goldstein reasoned "this is not a phenomenon amenable to randomized, control, double blind investigations given the rarity of both anti-GBM disease and significant adverse vaccine reactions." Pet. Ex. 45 at 2. He opined "[i]nsufficient and inadequate data are not the equivalent of proof that there is

[26] Dr. Goldstein provided two expert reports. Pet. Exs. 16, 45.

[27] Inst. of Med., Influenza Vaccine, in Adverse Effects of Vaccines: Evidence and Causality 293, 383 (Kathleen Stratton et al. eds., 2012).

no causal connection between vaccination and Goodpasture's [s]yndrome." Id. Dr. Goldstein further asserted that "[a]llowance must be made in this case for the possibility of novel biological events." Id.

In support of his opinions, Dr. Goldstein cited articles about anti-GBM disease. McAdoo and Pusey explained that anti-GBM disease "is a rare small vessel disease that affects the capillary beds of the kidneys and lungs." Pet. Ex. 22 at 1. In the kidneys, it causes glomerular necrosis, and in the lungs, it affects the pulmonary capillaries and may lead to alveolar hemorrhage. Id. The illness has been associated with cigarette smoking and hydrocarbon inhalation, and more recently, with alemtuzumab,[28] a treatment for multiple sclerosis. Id. at 2. An association with infections has also been reported, although the "causative nature of these associations [] is not proven and remains speculative." Id. The authors stated that environmental triggers may act in concert with genetics to trigger the illness. Id. Also, it is an autoimmune illness, where pathogenic autoantibodies target an "autoantigen expressed in the basement membranes of [kidneys and lungs], although the inciting events that induce[] the autoimmune response are not fully understood."[29] Id. at 1. The authors did not discuss any association between vaccines and anti-GBM disease.

In addition, Dr. Goldstein cited Norton et al.[30] who reported the case of a patient with double seropositive (ANCA and anti-GBM) vasculitis[31] that occurred after receipt of a flu vaccine. Pet. Ex. 16 at 4 (citing Pet. Ex. 27 at 1). The patient felt "generally unwell" four days after vaccination and was treated with antibiotics for a respiratory tract infection. Pet. Ex. 27 at 2. He subsequently developed hematuria and presented to the hospital four weeks after vaccination with high creatinine and positive ANCA and anti-GBM antibodies. Id. Renal biopsy was diagnostic for anti-GBM disease. Id. Given the temporal association with vaccination, the authors hypothesized the flu vaccine "may have caused an immunological response that stimulated an inflammatory process leading to double seropositive vasculitis and [acute kidney injury]" in a susceptible patient, "although a causal relationship [could not] be

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[28] Alemtuzumab is "a recombinant, DNA-derived, humanized monoclonal antibody directed against the CD antigen CD52, which is present on B and T lymphocytes, many monocytes, macrophages, and NK cells, and certain granulocytes." Alemtuzumab, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=1635 (last visited May 13, 2024).

[29] For a discussion of the immunopathogenesis of anti-GBM disease, see Pet. Ex. 22 at 3.

[30] Benjamin Norton et al., Vaccine: Friend or Foe? Double Seropositive Vasculitis Following Influenza Vaccination, 5 Oxford Med. Case Reps. 202 (2019).

[31] "Co-presentation with ANCA and anti-GBM antibodies represents double seropositive vasculitis, which accounted for up to 50% of patients presenting with anti-GBM in one cohort. Outcomes in double seropositive vasculitis are variable and represent a mixture between the clinical courses of both vasculitides." Pet. Ex. 27 at 1. Petitioner was not double seropositive, as she did not test positive for ANCA antibodies.

proved." Id. at 1, 3. The authors further noted that the etiology of the illness was unknown. Id. at 2. They offered two hypotheses: molecular mimicry (where vaccine antigens share structural similarities with self-antigens causing autoimmune condition) and adjuvants ("autoimmune syndrome induced by adjuvants"). Id. They concluded that the etiology was unclear. Id.

Dr. Goldstein also cited medical literature[32] to show that other autoimmune vasculitic conditions, beyond Goodpasture's syndrome, have been reported following flu vaccination. Pet. Ex. 16 at 4-5. Patel and Shah[33] reviewed renal complications that have been reported after vaccination, including after flu vaccination. Pet. Ex. 25 at 1. The authors stated that flu vaccines have been reported to be associated with nephrotic syndrome, rhabdomyolysis, renal vasculitis, Henoch-Schönlein purpura,[34] kidney graft rejection, nephrotic syndrome, minimal change disease,[35] membranous nephropathy,[36] acute tubular necrosis,[37] acute interstitial nephritis, and glomerulonephritis. Id. at 2 tbl.1, 2-4. Patel and Shah did not report any case of anti-GBM

[32] Dr. Goldstein also cited an abstract about anti-GBM glomerulonephritis, suggesting that a T cell-mediated mechanism may play a possible role is disease causation. See Pet. Ex. 21 (Ya-Huan Lou, Anti-GBM Glomerulonephritis: A T Cell-Mediated Autoimmune Disease?, 52 Archivum immunologiae et therapiae experimentalis 96 (2004)). Since only the abstract was filed, the undersigned does not discuss this article.

[33] Chinmay Patel & Hitesh H. Shah, Vaccine-Associated Kidney Disease: A Narrative Review of the Literature, 30 Saudi J. Kidney Disease & Transplantation 1002 (2019).

[34] Henoch-Schönlein purpura or allergic purpura is "a form of nonthrombocytopenic purpura, sometimes a type of hypersensitivity vasculitis and sometimes of unknown cause, usually seen in children and associated with symptoms including urticaria, erythema, arthropathy, arthritis, gastrointestinal symptoms, and renal involvement." Henoch-Schönlein Purpura, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=101148 (last visited May 10, 2024).

[35] Minimal change disease is "subtle alterations in kidney function demonstrable by clinical albuminuria and the presence of lipid droplets in cells of the proximal tubules; abnormalities of foot processes of the glomerular epithelial cells are present but too subtle to be seen with light microscopy." Minimal Change Disease, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=70603 (last visited Apr. 15, 2024).

[36] Membranous nephropathy is a "glomerulonephritis characterized histologically by proteinaceous deposits on the [GBM] or by thickening of the membrane, with circulating antigen-antibody complexes indicating immune complex disease." Membranous Glomerulonephritis, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=79021 (last visited Apr. 15, 2024).

[37] Acute tubular necrosis is "acute renal failure with mild to severe damage or necrosis of tubule cells." Acute Tubular Necrosis, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=91550 (last visited Apr. 15, 2024).

disease following flu vaccination (one was reported following a pneumococcal vaccine). Id. at 2 tbl.1, 5. Dr. Goldstein opined "[t]hese conditions share with Goodpasture's [syndrome] an autoimmune mechanism of injury credibly triggered by immune stimulation in the setting of [flu] vaccination." Pet. Ex. 16 at 5. However, Dr. Goldstein did not describe or explain how the flu vaccine can cause anti-GBM disease. And Patel and Shah did not describe any mechanism by which the flu vaccine can cause anti-GBM disease, instead noting that "the pathogenesis of the vaccine related renal manifestations is beyond the scope of the article." Pet. Ex. 25 at 3.

Jeffs et al.[38] reported the case of a patient who developed ANCA-associated vasculitis following a flu vaccine. Pet. Ex. 40 at 1. To investigate whether there was an association between ANCA-associated vasculitis and flu vaccination, the authors studied the ability of different types of flu vaccines to "stimulate proteinase-3 ANCA (PR3-ANCA) production in vitro." Id. at 1, 4. They found that only vaccines containing viral ribonucleic acid ("RNA") had the ability to stimulate PR3-ANCA. Id. at 1. The authors suggested that a "hyper-reaction to viral RNA in the [] vaccine may have contributed to the development of [ANCA-associated vasculitis]." Id. The patient was ANCA positive and had microscopic polyangiitis,[39] a different illness than anti-GBM/Goodpasture's syndrome. See id. at 1-2. Based on information in the article, it appears the patient received the split virion influenza vaccine for 2007 (ISV2), not the vaccine at issue here. Id. at 2. Moreover, there is no foundational evidence here to show that the flu vaccine at issue contained RNA.[40]

Although Dr. Goldstein opined Jeffs et al. established "a credible mechanism by which [the flu] vaccination may induce autoantibodies and autoimmune vasculitis," he did not explain how the study was relevant in the context of an anti-GBM illness when there is no ANCA-associated vasculitis. Pet. Ex. 16 at 5.

Regarding infectious triggers, Dr. Goldstein cited an article that reported a case of anti-GBM/Goodpasture's syndrome with primary involvement of the lungs following a respiratory infection. Pet. Ex. 16 at 4 (citing Pet. Ex. 26).[41] Wilson and Smith described a woman who

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[38] Lisa S. Jeffs et al., Viral RNA in the Influenza Vaccine May Have Contributed to the Development of ANCA-Associated Vasculitis in a Patient Following Immunisation, 35 Clinical Rheumatology 943 (2016).

[39] Microscopic polyangiitis is "a type of small vessel vasculitis, usually in the kidneys but sometimes also in the lungs, skin, and nervous system; characteristics are similar to those of polyarteritis nodosa with focal segmental glomerulosclerosis and presence of antineutrophil cytoplasmic autoantibodies." Microscopic Polyangiitis, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=99263 (last visited May 10, 2024).

[40] Petitioner received the Flulaval Quadrivalent 2016-2017 flu vaccine manufactured by Glaxo Smith Kline. See Pet. Ex. 2 at 3.

[41] Curtis B. Wilson & Robert C. Smith, Goodpasture's Syndrome Associated with Influenza A2 Virus Infection, 76 Annals Internal Med. 91 (1972).

developed pulmonary manifestations of anti-GBM/Goodpasture's syndrome after a presumed viral flu infection. Pet. Ex. 26 at 1. The patient had lung involvement with active hemoptysis[42] and "massive bilateral pulmonary infiltrates" but only a mild glomerular renal injury. Id. at 2-3. The authors opined that any association between the patient's prior flu infection and her anti-GBM illness "may have been coincidental." Id. at 3. They also suggested several theories about how the flu infection may have played a causal role such as "increas[ing] circulating basement membrane antigens, alter[ing] these antigens, or produc[ing] [] neoantigens that could cross-react with the GBM, resulting in the anti-GBM antibody response." Id. To presumably suggest that if the virus can cause the illness, so can the vaccine, Dr. Goldstein quoted the IOM which "consider[ed] the effects of natural infection [as] one type of mechanistic evidence." Pet. Ex. 16 at 4 (quoting Pet. Ex. 32 at 42).[43]

Respondent's experts distinguished the flu infection from the flu vaccination as a trigger for Goodpasture's syndrome, explaining that the flu infection would damage the lung, "exposing the otherwise culpable cryptic epitopes." Pet. Ex. 45 at 2. Although Dr. Goldstein agreed this position was reasonable, he argued it was "recklessly speculative in the absence of any actual supporting data." Id. By way of example, he noted it "has been suspected and observed for at least seven years that . . . alemtuzumab [] may lead to the development of anti-GBM disease. These observations have been sufficient to require a black box warning to this effect in the package insert for the drug." Id. He explained that "[a]lemtuzumab, unlike cigarette smoking, hydrocarbon inhalation[,] or clinical [flu] infection, cannot be regarded as an agent of structural lung damage leading to the exposure of cryptic epitopes directly causing antibody and disease development." Id. Dr. Goldstein concluded the actual mechanism of injury here "is unknown but clearly different from other accepted triggers of anti-GBM disease." Id.

ii. Althen Prongs Two and Three

Dr. Goldstein opined Petitioner had no "antecedent renal disease" and no "other risk factors" for anti-GBM /Goodpasture's syndrome. Pet. Ex. 16 at 3; see also Pet. Ex. 45 at 2. He suggested "the possibility that [] Petitioner had subclinical or smoldering anti-GBM disease (a known phenomenon) which, but for the immune stimulation of the vaccine, would not have blossomed into clinical Goodpasture's [s]yndrome." Pet. Ex. 45 at 3-4. He did not explain this possibility further. He explained that smoking and hydrocarbon exposure are risk factors for the disease, but Petitioner did not have these risks, and so she was not in a high-risk demographic. Pet. Ex. 16 at 3-4. Additionally, he opined Petitioner had no evidence of underlying renal disease prior to October 2016. Id. at 3.

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[42] Hemoptysis is "the expectoration of blood or of blood-stained sputum." Hemoptysis, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=22096 (last visited May 13, 2024).

[43] The section of the IOM report quoted is on the flu vaccine and Guillain-Barré syndrome ("GBS") not anti-GBM/Goodpasture's syndrome. Pet. Ex. 32 at 42. GBS is a "rapidly progressive ascending motor neuron paralysis of unknown etiology, frequently seen after an enteric or respiratory infection." Guillain-Barré Syndrome, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=110689 (last visited Apr. 15, 2024).

As for temporality, Dr. Goldstein opined Petitioner "developed symptoms beginning 24 hours following vaccination and reach[ed] a crescendo at ten days following vaccination." Pet. Ex. 16 at 3. To show the significance of this timeframe, Dr. Goldstein cited Watanbe,[44] which reviewed medical literature that, in total, described 65 cases of vasculitis following vaccination. Id. (citing Pet. Ex. 46 at 1). According to Dr. Goldstein, "the median duration of time from vaccination to presentation of vasculitis was 12 days," and "[a]lmost half of all patients developed vasculitis less than [two] weeks following vaccination." Id. He asserted that Petitioner's "chronology fits exactly with these published cases." Id. Additionally, Dr. Goldstein stated that the IOM considered temporality as a significant factor in determining association. Id. (citing Pet. Ex. 32 at 53).[45]

2. Petitioner's Expert, Gourang P. Patel, Ph.D.[46]

a. Background and Qualifications

Dr. Patel is "practicing clinical pharmacist" in the areas of pharmacy and pharmacology/toxicology at the University of Chicago. Pet. Ex. 17 at 1. He is not a medical doctor. He received his doctorate in pharmacy from the St. Louis College of Pharmacy in St. Louis, Missouri, and thereafter completed an internal medicine residency at John Cochran VA Medical Center. Pet. Ex. 31 at 1-2. He is currently a Clinical Pharmacist in Critical Care in the Department of Pharmacy at the University of Chicago. Pet. Ex. 31a at 1. Dr. Patel has 18 years of experience in clinical pharmacology "in a practice based academic medical setting." Pet. Ex. 17 at 1. His practice areas "include pharmacology/toxicology, medication adverse event investigation, and monitoring of medication therapy post administration." Id. He is "familiar with the [flu] vaccine preparations and the pharmacology/toxicology of these medications, including their effects on the human body and their subsequent sequela in patients." Id. Dr. Patel has co-authored textbook chapters, peer-reviewed articles, and presentations. Pet. Ex. 31 at 4-12.

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[44] Toru Watanabe, Vasculitis Following Influenza Vaccination: A Review of the Literature, 13 Current Rheumatology Revs. 188 (2017).

[45] Regarding the significance of temporality, Dr. Goldstein cited the section of the IOM report on the flu vaccine and anaphylaxis, not the flu vaccine and anti-GBM/Goodpasture's syndrome. Anaphylaxis is "a type I hypersensitivity reaction in which exposure of a sensitized individual to a specific antigen or hapten results in urticaria, pruritus, and angioedema, followed by vascular collapse and shock and often accompanied by life-threatening respiratory distress." Anaphylaxis, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=2577 (last visited May 10, 2024). Dr. Goldstein did not reference anaphylaxis as a potential mechanism at issue herein.

[46] Dr. Patel provided one expert report. Pet. Ex. 17.

b. Causation Opinion

Dr. Patel opined "the administration of the [flu] vaccine given to [Petitioner] was a significant contributing factor in causing her small vessel vasculitis." Pet. Ex. 17 at 3. His opinion related to the mechanism of causation is as follows.

Dr. Patel stated that "[i]nactivated [flu] vaccines are standardized to contain the hemagglutinins[47] that represent the virus types likely to be circulating . . . during the incoming [flu] season." Pet. Ex. 17 at 2. He explained that the Fluarix[48] flu vaccine contains both flu A and B virus subtypes. Id. (citing Pet. Ex. 42). After vaccination, exposure to the antigens in the vaccine "initiates a cascade of reactions involving the immune system activating white blood cells called lymphocytes (B-cells and T-cells) that are utilized to fight off an infection." Id. According to Dr. Patel, it generally takes seven to 10 days to develop an antibody response, although he explained that adverse reactions have been reported "shortly outside" of this time frame. Id.

For support that vaccines can cause vasculitis, Dr. Patel cited case reports by Blumberg et al.[49] and Zafrir et al.[50] Pet. Ex. 17 at 2 (citing Pet. Exs. 41, 44). Blumberg et al. described two cases. Pet. Ex. 41 at 1. The first patient had "fever, arthralgia, and myalgias 11 days" after vaccination, and subsequently developed blurry vision and left eye pain. Id. He was diagnosed with iritis[51] in one eye and optic neuritis[52] in the other. Id. The second patient had "fever, malaise, generalized arthralgia, myalgias, and swollen lips" occurring several hours after

[47] Hemagglutinin is an antibody or other substance that causes red blood cells (erythrocytes) to clump together (agglutinate). Hemagglutinin, Stedman's Med. Dictionary 861 (28th ed. 2006).

[48] Petitioner did not receive the Fluarix vaccine; she received the Flulaval flu vaccine. Pet. Ex 2 at 1-2. Dr. Patel did not explain if or how Flulaval and Fluarix are related. However, for purposes of this Decision, the undersigned presumes there is no substantial difference in the vaccines.

[49] Scott Blumberg et al., A Possible Association Between Influenza Vaccination and Small-Vessel Vasculitis, 140 Archives Internal Med. 847 (1980).

[50] Yaron Zafrir et al., Post-Influenza Vaccination Vasculitides, 15 J. Clinical Rheumatology 269 (2009).

[51] Iritis is "inflammation of the iris, usually marked by pain, congestion in the ciliary region, photophobia, contraction of the pupil, and discoloration of the iris." Iritis, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=26154 (last visited May 13, 2024).

[52] Optic neuritis is "inflammation of the optic nerve; it is classified as either intraocular, affecting the part of the nerve within the eyeball[,] or retrobulbar, affecting the portion behind the eyeball." Optic Neuritis, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=92519 (last visited May 10, 2024).

vaccination. Id. Two days later he had a purpuric[53] rash of the trunk and extremities. Id. Biopsy showed "cutaneous necrotizing vasculitis"[54] of the "papillary dermis."[55] Id. The patient had a past history of "allergic purpura" associated with a URI. Id. at 1-2. Regarding causation, the authors concluded it was "conceivable that an immunologic pathogenesis with tissue deposition of immune complexes containing putative antigens from the [flu] vaccine could lead to [] illness." Id. at 2. Neither case report related to anti-GBM/Goodpasture's syndrome.

Zafrir et al. discussed another article that reported three cases of adults with new onset and one with relapse of ANCA-associated vasculitis post-vaccination. Pet. Ex. 44 at 1. Onset of symptoms occurred 12 to 21 days post-vaccination (a latency period "within the classic time frame suggested for . . . postvaccination autoimmunity"). Id. at 1-2. The authors stated that the "association between vaccination and autoimmunity may be mediated through several mechanisms which include immune mediated responses to the infectious antigen or other excipients of each vaccine." Id. at 2. The authors concluded there was a "possibility of a causal link" between flu vaccines and vasculitic illnesses. Id.

Lastly, Dr. Patel discussed the temporal association of Petitioner's presentation in relation to her vaccination by referencing Watanabe's review of medical literature related to vasculitis (including giant cell arteritis, Takayasu arteritis, polyarteritis nodosa, Kawasaki disease, microscopic polyangiitis, granulomatosis with polyangiitis, eosinophilic granulomatosis with polyangiitis, and IgA vasculitis). Pet. Ex. 17 at 2 (citing Pet. Ex. 46). Anti-GBM/Goodpasture's syndrome-associated vasculitis was not included in the review. See Pet. Ex. 46. Acute kidney injury was reported in seven patients (although these appear to be due to microscopic polyangiitis and/or granulomatosis with polyangiitis or other forms of vasculitis not

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[53] Purpuric is "of the nature of, pertaining to, or affected with purpura." Purpuric, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=42171 (last visited May 15, 2024). Purpura refers to "any of a group of conditions characterized by ecchymoses or other small hemorrhages in the skin, mucous membranes, or serosal surfaces; causes include blood disorders, vascular abnormalities, and trauma." Purpura, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=42170 (last visited May 15, 2024).

[54] Cutaneous vasculitis is "an acute form of v[asculitis] that may affect the skin only, but also may involve other organs, with a polymorphonuclear infiltrate in the walls of and surrounding small (dermal) vessels." Cutaneous Vasculitis, Stedman's Med. Dictionary 2092 (28th ed. 2006). Necrotizing vasculitis or systemic vasculitis refers to "any of a group of disorders characterized by inflammation and necrosis of blood vessels, occurring in a broad spectrum of cutaneous and systemic disorders." Systemic Vasculitis, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=116920 (last visited May 15, 2024).

[55] Papillary dermis is the "papillary layer: the outer layer of the dermis, characterized by ridges or papillae protruding into the epidermis, and by greater cellularity and vascularization than the reticular layer of the dermis." Stratum Papillare Dermidis, Dorland's Med. Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=108706 (last visited May 10, 2024).

at issue here). Id. at 2, 5. The "median duration of time from vaccination to presentation of vasculitis was 12 days (0-90 days)." Id. at 3. Dr. Patel opined Petitioner "presented 11 days post vaccination which is well within the temporal range expected for this clinical adverse event." Pet. Ex. 17 at 2. Although Dr. Patel noted the day that Petitioner presented to a healthcare provider, he did not provide an opinion as to what symptom constituted Petitioner's first manifestation of anti-GBM/Goodpasture's syndrome or the date of such symptom.

3. Respondent's Expert, Dr. George Jarad, M.D.[56]

a. Background and Qualifications

Dr. Jarad is a board-certified nephrologist. Resp. Ex. B at 1. He received his M.D. at Damascus University and completed an internal medicine residency and fellowship at Case Western Reserve University, University Hospital/VA of Cleveland, and MetroHealth Medical Center in Cleveland, Ohio. Resp. Ex. C at 1. Thereafter, he completed a post-doctoral fellowship in the renal division at the Washington University School of Medicine in St. Louis, Missouri. Id. Dr. Jarad is currently an Associate Professor of Internal Medicine and Nephrology at Washington University School of Medicine, "with primary interest in proteinuric kidney diseases and significant experience in GBM diseases, especially type [four] Collagen (Collagen IV) diseases." Resp. Ex. B at 1. He is also the Medical Director of the Forest Mark Dialysis Center at the Washington University School of Medicine. Resp. Ex. C at 1. In his clinical practice and referral center, he encounters "multiple cases of [RPGN] including anti-GBM/Goodpasture disease on monthly bases." Resp. Ex. B at 1. Dr. Jarad has authored or co-authored numerous publications. Resp. Ex. C at 2-3.

b. Causation Opinion

Dr. Jarad agreed that Petitioner's diagnosis is anti-GBM/Goodpasture's syndrome. Resp. Ex. B at 10. However, Dr. Jarad opined that Petitioner's experts failed to articulate a mechanism to explain how the flu vaccine can induce anti-GBM/Goodpasture's syndrome. Id. at 3. He also opined that Petitioner did not present "reliable, persuasive evidence of a causal relationship between the quadrivalent [flu] vaccine and the development of anti-GBM disease." Id. at 11.

i. Althen Prong One

Dr. Jarad explained the current understanding about the pathogenesis of anti-GBM disease/Goodpasture's syndrome. Resp. Ex. B at 8. He defined anti-GBM disease as "an autoimmune disease that can affect kidney and lung," although the illness can be limited to the kidney. Id. The clinical presentation of the disease can be explained by the "distribution of specific Collagen IV molecules and generation of autoantibodies." Id. "Anti-GBM antibodies are targeted against . . . epithelial cells in the kidney filter ([g]lomerulus)" called the GBM. Id. It contains "multiple molecules belonging [to] different families, including Collagen IV." Id. Although much is known about "the target epitopes of the autoantibodies in anti-GBM disease," Dr. Jarad noted that "there are many unanswered questions about the cause of the disease[]." Id.

[56] Dr. Jarad provided one expert report. Resp. Ex. B.

Dr. Jarad described the Collagen IV family of molecules that form mature mesh-like structures. Resp. Ex. B at 8. The most common antibody is targeted against the noncollagenous domain1 ("NC1") of the Collagen IV α3 chain and the Collagen IV α5 chain. Id. "Such domains are considered to be 'immune privileged' or 'cryptic'" because "due to the complex interaction of the Collagen IV chains[,] they are protected from the immune system." Id. He stated that "it is not always clear what breaks this tight bond and expose[s] the cryptic antigen to the immune system." Id. For "an event to induce anti-GBM disease it is not enough to disrupt the links between Collagen IV molecules, sensitize B and T lymphocytes, and generate an autoantibody." Id. "It is also crucial for such an event to maintain the disruption of the Collagen IV molecules and continue to expose the cryptic antigen to further attack by the immune system." Id. (emphasis omitted). Moreover, in some patients, the anti-GBM antibody can be detected years before disease manifestation. Id. at 9.

Due to these complexities, Dr. Jarad opined that the "cause of most cases of anti-GBM remains a mystery." Resp. Ex. B at 9. He agreed with the literature cited by Petitioner's experts stating that smoking and hydrocarbon exposure may be "potential triggers." Id. He also agreed there is an association between respiratory infections and the disease, and he offered literature to show there was an increase in the illness associated with Covid-19 infections. Id. (citing Resp. Ex. B, Tab 8).[57] However, he opined that the association between vaccination and anti-GBM disease "is not well established" and has "not been suggested based on expert opinion." Id. "There is a fundamental difference between [flu] infection and vaccination. What is known about the relationship between [Goodpasture's syndrome], and [flu] infection cannot be extrapolated to the [flu] vaccination that [P]etitioner received." Id. at 10.

Dr. Jarad reviewed the literature referenced by Petitioner's experts but opined none of the papers establish a causal relationship between flu vaccination and anti-GBM/Goodpasture's syndrome. Resp. Ex. B at 3-8.[58] For example, Patel and Shah only reported one case of anti-GBM disease after a pneumococcal vaccination, and none after a flu vaccination. Id. at 4 (citing Pet. Ex. 25).

According to Dr. Jarad, Norton et al. described a patient who developed double seropositive vasculitis following a flu vaccine and "overemphasized the role of the vaccine while under-appreciating the role of a possible association with respiratory infection." Resp. Ex. B at 4 (citing Pet. Ex. 27). The patient had symptoms four days after vaccination and was initially treated with antibiotics for a presumed lower respiratory tract infection. Id. (citing Pet. Ex. 27 at 2). "Despite the presence of pulmonary symptoms, there was no pulmonary manifestation of anti-GBM/Goodpasture['s] [syndrome]." Id. Therefore, Dr. Jarad opined the authors "did not provide sufficient explanation for the lower respiratory symptoms." Id.

[57] Allan Sacker et al., Anti-GBM Nephritis with Mesangial IgA Deposits After SARS-CoV-2 mRNA Vaccination, 100 Kidney Int'l 471 (2021).

[58] For Dr. Jarad's specific opinions about each article cited by Petitioner, see Resp. Ex. B at 3-8.

Dr. Jarad took issue with Jeffs et al., which found that viral RNA in the flu vaccine "may have contributed to the development of [ANCA-associated vasculitis] following [flu] vaccination in [their] patient." Resp. Ex. B at 7 (quoting Pet. Ex. 40 at 1). However, "viral RNA is not universal throughout all vaccines." Id. (citing Pet. Ex. 40 at 1). Some of the vaccines tested did not contain viral RNA. Id. Importantly, Dr. Jarad pointed out that the authors did not test the vaccine at issue in this case. Id. He concluded that "[e]ven if we accept the finding, the study tested the production of PR3-ANCA [ANCA-related disease], not anti-GBM antibody, which makes the results less relevant [here]." Id.

Duggal et al.[59] reported two cases of ANCA-associated vasculitis within two and four weeks of flu vaccination. Pet. Ex. 35 at 1. The authors concluded a causal role could not be confirmed even though there was a temporal association. Id. Dr. Jarad explained that while ANCA-associated vasculitis and anti-GBM disease share common manifestations, such as kidney and lung involvement and the presence of auto-antibodies (albeit, different types), there are stark differences in the mechanism of the diseases. Resp. Ex. B at 6. He concluded that "[e]ven if we . . . accept the causal relationship between [flu] vaccination and the development of ANCA vasculitis and vaccination, such a conclusion cannot be extended to anti-GBM/Goodpasture['s] [syndrome]." Id. He further explained that the "[flu] virus affects the lung and can disrupt the structure of the Collagen IV molecule exposing its cryptic antigen to the immune system." Id. at 10. This is different than a process that does not trigger lung injury at the onset such as kidney limited anti-GBM/Goodpasture's syndrome. Id.

ii. Althen Prongs Two and Three

Dr. Jarad agreed with Petitioner's diagnosis of anti-GBM/Goodpasture's syndrome. Resp. Ex. B at 9. Petitioner's kidney failure, hematuria, proteinuria, high anti-GBM titers, and the kidney biopsy, "especially the linear staining of the GBM with IgG," are all diagnostic of the disease. Id. at 9-10.

However, Dr. Jarad opined Petitioner's initial presenting symptoms were not typical for kidney limited anti-GBM disease. Resp. Ex. B at 11. Petitioner's "clinical presentation . . . started within the first day after receiving the vaccine and included a [two]-week course of a mix of upper and lower respiratory symptoms." Id. at 10. Because there was no evidence of pulmonary involvement, Dr. Jarad opined Petitioner's kidney limited anti-GBM/Goodpasture's syndrome cannot explain all of her presenting symptoms such as the upper and lower respiratory symptoms. Id.

As for timing, Dr. Jarad opined Petitioner's start of symptoms began "within the first day after receiving the vaccine and included a [two]-week course of a mix of upper and lower respiratory symptoms (with some similarities to the case report in [Wilson and Smith])." Resp. Ex. B at 10 (citing Pet. Ex. 26). He opined that an onset of one day after vaccination is too short to induce autoantibodies and T cell reactivity. Id. at 11.

[59] Tanu Duggal et al., Antineutrophil Cytoplasmic Antibody Vasculitis Associated with Influenza Vaccination, 38 Am. J. Nephrology 174 (2013).

Citing the portion of the IOM report filed by Petitioner, Dr. Jarad noted the latency phase between exposure and response is four to seven days for T cells and seven to 10 days for B cells. Resp. Ex. B at 5 (citing Pet. Ex. 34). Moreover, given the knowledge of disease pathogenesis, it usually takes "weeks, if not months" to begin "production of the autoantibody and the development of clinical disease." Id. at 10. For these reasons, he opined a 24-hour lag time "is not sufficient to disrupt the links between Collagen IV molecules, sensitize B and T lymphocytes, [] generate autoantibody, maintain the disruption of the Collagen IV molecules[,] and continue to expose the cryptic antigen to further attack by the immune system." Id. (emphasis omitted).

4. Respondent's Expert, Dr. Arnold I. Levinson, M.D.[60]

a. Background and Qualifications

Dr. Levinson is board certified in internal medicine and allergy and clinical immunology. Resp. Ex. D at 1; Resp. Ex. E at 2. He received his M.D. from the University of Maryland. Resp. Ex. E at 1. He completed fellowships at the Johns Hopkins Hospital and the University of Pennsylvania School of Medicine, and post-doctoral fellowships in immunology at the University of Pennsylvania School of Medicine and the University of California, San Francisco Medical Center. Id. Dr. Levinson is currently an Emeritus Professor of Medicine and Neurology at the Perelman School of Medicine at the University of Pennsylvania. Resp. Ex. D at 1. Over a period of 33 years, Dr. Levinson "conducted a clinical practice in which [he] evaluated and treated patients with a broad range of immune-mediated diseases including autoimmune, hypersensitivity, and immunodeficiency disorders." Id. Dr. Levinson has authored or co-authored numerous publications. Resp. Ex. E at 10-21.

b. Causation Opinion

Dr. Levinson agreed Petitioner suffered from Goodpasture's syndrome but disagreed that this syndrome was caused by her flu vaccine. Resp. Ex. D at 7. Like Dr. Jarad, Dr. Levinson believed Petitioner's experts failed to provide a biological mechanism of vaccine causation. Id.

i. Althen Prong One

Like Dr. Jared, Dr. Levinson defined Goodpasture's syndrome and explained its pathogenesis. Resp. Ex. D at 4. He agreed that the illness is an "inflammatory pulmonary-renal syndrome that largely affects the glomerular capillaries in the kidney and alveolar capillaries in the lung." Id. at 3. In the kidney, this is caused by "severe cellular proliferation" of "infiltrating leukocytes and [] glomerular epithelial cells." Id. at 4. Tissue damage is "mediated by an IgG autoantibody [] specific for a target antigen [] expressed on the basement membranes of both pulmonary and glomerular capillaries. That target is the non-collagenous domain of the α3 chain

[60] Dr. Levinson provided one expert report. Resp. Ex. D.

of type IV collagen [].”[61] Id. Tissue destruction is thought to be caused when “anti-GBM antibodies bound to the tissue-expressed epitopes activate the classical complement pathway. However, more recent studies have also implicated an important role of phagocytic cell [] receptors in the tissue destruction.” Id.

According to Dr. Levinson, Petitioner’s experts oversimplified the cause of vasculitis and “incorrectly implied that vasculitic disorders are caused by the deposition of circulating immune complexes into blood vessels.” Resp. Ex. D at 7. While Dr. Levinson agreed that deposition of circulating immune complexes into the vessels of some organs is responsible for some types of vasculitis,[62] this process does not occur in many vasculitic conditions, and importantly, it does not play a role in the pathogenesis of Goodpasture’s syndrome. Id. Therefore, Dr. Levinson opined that other types of vasculitis which have different causal mechanisms cannot be used to support vaccine-related causation here. Id. at 5.

This problem is further illustrated by Petitioner’s experts’ reliance on the Watanabe paper. Resp. Ex. D at 5, 7 (citing Pet. Ex. 46). Dr. Levinson noted that the goal of the article was to “identify patients who developed vasculitis following [flu] vaccination and to clarify the clinical manifestations of vasculitis in these patients.” Id. (quoting Pet. Ex. 46 at 1). Although the paper presented a spectrum of vasculitic syndromes, anti-GBM/Goodpasture’s syndrome was not included. Id. Most were examples of systemic vasculitis disorders, whereas anti-GBM/Goodpasture’s syndrome is a kidney and/or lung limited disease. Id. Moreover, as stated above, the pathogenesis of anti-GBM/Goodpasture’s syndrome is different from the small vessel vasculitic conditions reported in Watanabe. Id. at 5, 7 (citing Pet. Ex. 46). Dr. Levinson noted the paper by Patel and Shah raised the same concerns. Id. at 6-7 (citing Pet. Ex. 25). As such, he opined that the findings or conclusions of the papers cannot be extrapolated to this case. Id.

Dr. Levinson acknowledged the single case report by Norton et al. describing a case of double seropositive vasculitis following the flu vaccine cited by Dr. Goldstein. Resp. Ex. D at 6 (citing Pet. Ex. 27). Although Dr. Levinson agreed with the diagnosis in the case report, he opined that an onset of four days was too soon to implicate vaccine causation (described in more detail in prong three below). Id. Further, the authors did not make a causal association between vaccination and the illness. Id. Dr. Levinson opined that a single case report is insufficient to establish causation, especially given the large number of flu vaccines administered. Id.

Regarding Petitioner’s experts’ opinions based on assertions that flu infections can cause vasculitic disorders and literature cited for this proposition, Dr. Levinson raised several concerns. Resp. Ex. D at 6. While Dr. Levinson acknowledged the authors of Wilson and Smith supported

[61] For a more detailed discussion of pathogenesis, including the identification of the epitopes targeted by anti-GBM antibodies, as well as the role played by T cells, see Resp. Ex. D at 3-4.

[62] Examples of vasculitis types with a pathogenesis that involves the “deposition of circulating immune complexes into the vessels” of organs include, “hypersensitivity/leukocytoclastic vasculitis, hepatitis B associated polyarteritis nodosa, [and] mixed cryoglobulinemia.” Resp. Ex. D at 7.

a causal association related to infection, he disagreed that this association could be extended to vaccination. Id. (citing Pet. Ex. 26).

Further, Dr. Levinson noted that the patient in the eponymous case of Goodpasture's syndrome actually had systemic ANCA-associated vasculitis with involvement of the kidney, lungs, spleen, gastrointestinal tract. Resp. Ex. D at 6 (citing Resp. Ex. D, Tab 2).[63] Because Petitioner here did not have the same condition as the patient described in Dr. Goodpasture's 1919 article, Dr. Levinson opined that the pathogenesis was not relevant to the condition at issue here. Id. at 6-7 (citing Resp. Ex. D, Tab 2); see also Pet. Ex. 39 at 5 (explaining that the first case report of Goodpasture's syndrome, an 18-year-old who had pulmonary hemorrhage and glomerulonephritis after flu infection, "likely had [ANCA] antibody disease rather than true Goodpasture's").[64]

In conclusion, Dr. Levinson opined there is a "major gap" in Petitioner's theory because of "the lack of any biological mechanism explaining how the [flu] vaccine could have elicited the production of the deleterious IgG autoantibodies that target the [GBM] in [Goodpasture's syndrome]." Resp. Ex. D at 6.

ii. Althen Prongs Two and Three

Dr. Levinson reviewed Petitioner's clinical course noting that Petitioner placed onset of her symptoms ("malaise, chills[,] and night sweats") within 24 hours of her flu vaccination. Resp. Ex. D at 2. Her illness progressed, and she had loss of appetite, nausea, vomiting, and hematuria about one week after receiving her vaccine. Id. Medical records evidenced that she also complained of chest pain when taking deep breaths, nasal congestion, cough, and sweating two weeks before she presented for treatment. Id. On admission to the hospital on October 27, 2016, Petitioner reported symptoms of an URI two weeks before admission. Id. at 3. The records also confirmed that Petitioner was positive for the anti-GBM antibody, "the classical autoantibody" in Goodpasture's syndrome. Id.

Because Dr. Levinson opined "the action of IgG anti-GBM antibodies is central to the pathogenesis" of Goodpasture's syndrome, he considered how the flu vaccine "might influence production of this antibody that triggers the cascade of events that lead to glomerular injury." Resp. Ex. D at 5 (citing Pet. Ex. 22; Resp. Ex. D, Tab 3;[65] Pet. Ex. 37).[66] Dr. Levinson opined it takes "several days" for IgG antibodies to appear in response to a primary immunization and

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[63] Sally Self, Goodpasture's 1919 Article on the Etiology of Influenza—The Historical Road to What We Now Call Goodpasture Syndrome, 338 Am. J. Med. Scis. 154.

[64] Toru Watanabe, Renal Complications of Seasonal and Pandemic Influenza A Virus Infections, 172 Eur. J. Pediatrics 15 (2013).

[65] Antonio Greco et al., Goodpasture's Syndrome: A Clinical Update, 14 Autoimmunity Revs. 246 (2015).

[66] Vadim Pedchenko et al., Goodpasture's Autoimmune Disease – A Collagen IV Disorder, 71-72 Matrix Biology 240 (2018).

longer than two or three days following secondary immunization. Id. (citing Pet. Ex. 32). He added "it would take additional days after the appearance of the pathologic antibodies in serum for them to act on the targeted tissue and cause injury." Id. at 6. "Therefore, given the fact that anti-GBM antibodies would definitely not be expected to have been produced in 24 hours," Dr. Levinson opined "it seems extremely unlikely that her disease was caused by the [flu] vaccine." Id.

III. DISCUSSION

A. Standards for Adjudication

The Vaccine Act was established to compensate vaccine-related injuries and deaths. § 10(a). "Congress designed the Vaccine Program to supplement the state law civil tort system as a simple, fair and expeditious means for compensating vaccine-related injured persons. The Program was established to award 'vaccine-injured persons quickly, easily, and with certainty and generosity.'" Rooks v. Sec'y of Health & Hum. Servs., 35 Fed. Cl. 1, 7 (1996) (quoting H.R. Rep. No. 908 at 3, reprinted in 1986 U.S.C.C.A.N. at 6287, 6344).

Petitioner's burden of proof is by a preponderance of the evidence. § 13(a)(1). The preponderance standard requires a petitioner to demonstrate that it is more likely than not that the vaccine at issue caused the injury. Moberly v. Sec'y of Health & Hum. Servs., 592 F.3d 1315, 1322 n.2 (Fed. Cir. 2010). Proof of medical certainty is not required. Bunting v. Sec'y of Health & Hum. Servs., 931 F.2d 867, 873 (Fed. Cir. 1991). Petitioner need not make a specific type of evidentiary showing, i.e., "epidemiologic studies, rechallenge, the presence of pathological markers or genetic predisposition, or general acceptance in the scientific or medical communities to establish a logical sequence of cause and effect." Capizzano v. Sec'y of Health & Hum. Servs., 440 F.3d 1317, 1325 (Fed. Cir. 2006). Instead, Petitioner may satisfy her burden by presenting circumstantial evidence and reliable medical opinions. Id. at 1325-26.

In particular, a petitioner must prove that the vaccine was "not only [the] but-for cause of the injury but also a substantial factor in bringing about the injury." Moberly, 592 F.3d at 1321 (quoting Shyface v. Sec'y of Health & Hum. Servs., 165 F.3d 1344, 1352-53 (Fed. Cir. 1999)); see also Pafford v. Sec'y of Health & Hum. Servs., 451 F.3d 1352, 1355 (Fed. Cir. 2006). The received vaccine, however, need not be the predominant cause of the injury. Shyface, 165 F.3d at 1351. A petitioner who satisfies this burden is entitled to compensation unless Respondent can prove, by a preponderance of the evidence, that the vaccinee's injury is "due to factors unrelated to the administration of the vaccine." § 13(a)(1)(B). However, if a petitioner fails to establish a prima facie case, the burden does not shift. Bradley v. Sec'y of Health & Hum. Servs., 991 F.2d 1570, 1575 (Fed. Cir. 1993).

"Regardless of whether the burden ever shifts to the [R]espondent, the special master may consider the evidence presented by the [R]espondent in determining whether the [P]etitioner has established a prima facie case." Flores v. Sec'y of Health & Hum. Servs., 115 Fed. Cl. 157, 162-63 (2014); see also Stone v. Sec'y of Health & Hum. Servs., 676 F.3d 1373, 1379 (Fed. Cir. 2012) ("[E]vidence of other possible sources of injury can be relevant not only to the 'factors unrelated' defense, but also to whether prima facie showing has been made that the vaccine was

a substantial factor in causing the injury in question."); de Bazan v. Sec'y of Health & Hum. Servs., 539 F.3d 1347, 1353 (Fed. Cir. 2008) ("The government, like any defendant, is permitted to offer evidence to demonstrate the inadequacy of the [P]etitioner's evidence on a requisite element of the [P]etitioner's case-in-chief."); Pafford, 451 F.3d at 1358-59 ("[T]he presence of multiple potential causative agents makes it difficult to attribute 'but for' causation to the vaccination. . . . [T]he Special Master properly introduced the presence of the other unrelated contemporaneous events as just as likely to have been the triggering event as the vaccinations.").

B. Factual Issues

Petitioner must prove, by a preponderance of the evidence, the factual circumstances surrounding her claim. § 13(a)(1)(A). To resolve factual issues, the special master must weigh the evidence presented, which may include contemporaneous medical records and testimony. See Burns v. Sec'y of Health & Hum. Servs., 3 F.3d 415, 417 (Fed. Cir. 1993) (explaining that a special master must decide what weight to give evidence including oral testimony and contemporaneous medical records).

Medical records, specifically contemporaneous medical records, are presumed to be accurate and generally "warrant consideration as trustworthy evidence." Cucuras v. Sec'y of Health & Hum. Servs., 993 F.2d 1525, 1528 (Fed. Cir. 1993). But see Kirby v. Sec'y of Health & Hum. Servs., 997 F.3d 1378, 1382 (Fed. Cir. 2021) (rejecting the presumption that "medical records are accurate and complete as to all the patient's physical conditions"); Shapiro v. Sec'y of Health & Hum. Servs., 101 Fed. Cl. 532, 538 (2011) ("[T]he absence of a reference to a condition or circumstance is much less significant than a reference which negates the existence of the condition or circumstance." (quoting Murphy v. Sec'y of Health & Hum. Servs., 23 Cl. Ct. 726, 733 (1991), aff'd per curiam, 968 F.2d 1226 (Fed. Cir. 1992))), recons. den'd after remand, 105 Fed. Cl. 353 (2012), aff'd mem., 503 F. App'x 952 (Fed. Cir. 2013). The weight afforded to contemporaneous records is due to the fact that they "contain information supplied to or by health professionals to facilitate diagnosis and treatment of medical conditions. With proper treatment hanging in the balance, accuracy has an extra premium." Id. To overcome the presumptive accuracy of medical records, a petitioner may present testimony which is "consistent, clear, cogent, and compelling." Sanchez v. Sec'y of Health & Hum. Servs., No. 11-685V, 2013 WL 1880825, at *3 (Fed. Cl. Spec. Mstr. Apr. 10, 2013) (citing Blutstein v. Sec'y of Health & Hum. Servs., No. 90-2808V, 1998 WL 408611, at *5 (Fed. Cl. Spec. Mstr. June 30, 1998)), mot. for rev. denied, 142 Fed. Cl. 247 (2019), vacated on other grounds & remanded, 809 F. App'x 843 (Fed Cir. 2020).

There are situations in which compelling testimony may be more persuasive than written records, such as where records are deemed to be incomplete or inaccurate. Campbell v. Sec'y of Health & Hum. Servs., 69 Fed. Cl. 775, 779 (2006) ("[L]ike any norm based upon common sense and experience, this rule should not be treated as an absolute and must yield where the factual predicates for its application are weak or lacking."); Lowrie v. Sec'y of Health & Hum. Servs., No. 03-1585V, 2005 WL 6117475, at *19 (Fed. Cl. Spec. Mstr. Dec. 12, 2005) ("[W]ritten records which are, themselves, inconsistent, should be accorded less deference than those which are internally consistent." (quoting Murphy, 23 Cl. Ct. at 733)). Ultimately, a determination regarding a witness's credibility is needed when determining the weight that such

testimony should be afforded. Andreu v. Sec'y of Health & Hum. Servs., 569 F.3d 1367, 1379 (Fed. Cir. 2009); Bradley, 991 F.2d at 1575.

Despite the weight afforded medical records, special masters are not bound rigidly by those records in determining onset of a petitioner's symptoms. Valenzuela v. Sec'y of Health & Hum. Servs., No. 90-1002V, 1991 WL 182241, at *3 (Fed. Cl. Spec. Mstr. Aug. 30, 1991); see also Eng v. Sec'y of Health & Hum. Servs., No. 90-1754V, 1994 WL 67704, at *3 (Fed. Cl. Spec. Mstr. Feb. 18, 1994) (Section 13(b)(2) "must be construed so as to give effect also to § 13(b)(1) which directs the special master or court to consider the medical records (reports, diagnosis, conclusions, medical judgment, test reports, etc.), but does not require the special master or court to be bound by them").

C. Causation

To receive compensation through the Program, Petitioner must prove either (1) that she suffered a "Table Injury"—i.e., an injury listed on the Vaccine Injury Table—corresponding to a vaccine that she received, or (2) that she suffered an injury that was actually caused by a vaccination. See §§ 11(c)(1), 13(a)(1)(A); Capizzano, 440 F.3d at 1319-20. Petitioner must show that the vaccine was "not only a but-for cause of the injury but also a substantial factor in bringing about the injury." Moberly, 592 F.3d at 1321 (quoting Shyface, 165 F.3d at 1352-53).

Because Petitioner does not allege she suffered a Table Injury, she must prove a vaccine she received actually caused her injury. To do so, Petitioner must establish, by preponderant evidence: "(1) a medical theory causally connecting the vaccination and the injury; (2) a logical sequence of cause and effect showing that the vaccination was the reason for the injury; and (3) a showing of a proximate temporal relationship between vaccination and injury." Althen, 418 F.3d at 1278.

The causation theory must relate to the injury alleged. Petitioner must provide a sound and reliable medical or scientific explanation that pertains specifically to this case, although the explanation need only be "legally probable, not medically or scientifically certain." Knudsen v. Sec'y of Health & Hum. Servs., 35 F.3d 543, 548-49 (Fed. Cir. 1994). Petitioner cannot establish entitlement to compensation based solely on her assertions; rather, a vaccine claim must be supported either by medical records or by the opinion of a medical doctor. § 13(a)(1). In determining whether Petitioner is entitled to compensation, the special master shall consider all material in the record, including "any . . . conclusion, [or] medical judgment . . . which is contained in the record regarding . . . causation." § 13(b)(1)(A). The special master must weigh the submitted evidence and the testimony of the parties' proffered experts and rule in Petitioner's favor when the evidence weighs in her favor. See Moberly, 592 F.3d at 1325-26 ("Finders of fact are entitled—indeed, expected—to make determinations as to the reliability of the evidence presented to them and, if appropriate, as to the credibility of the persons presenting that evidence."); Althen, 418 F.3d at 1280 (noting that "close calls" are resolved in Petitioner's favor).

Testimony that merely expresses the possibility—not the probability—is insufficient, by itself, to substantiate a claim that such an injury occurred. See Waterman v. Sec'y of Health &

Hum. Servs., 123 Fed. Cl. 564, 573-74 (2015) (denying Petitioner's motion for review and noting that a possible causal link was not sufficient to meet the preponderance standard). The Federal Circuit has made clear that the mere possibility of a link between a vaccination and a petitioner's injury is not sufficient to satisfy the preponderance standard. Moberly, 592 F.3d at 1322 (emphasizing that "proof of a 'plausible' or 'possible' causal link between the vaccine and the injury" does not equate to proof of causation by a preponderance of the evidence); Boatmon v. Sec'y of Health & Hum. Servs., 941 F.3d 1351, 1359-60 (Fed. Cir. 2019). While certainty is by no means required, a possible mechanism does not rise to the level of preponderance. Moberly, 592 F.3d at 1322; see also de Bazan, 539 F.3d at 1351.

IV. ANALYSIS

A. Althen Prong One

Under Althen prong one, Petitioner must set forth a medical theory explaining how the received vaccine could have caused the sustained injury. Andreu, 569 F.3d at 1375; Pafford, 451 F.3d at 1355-56. Petitioner's theory of causation need not be medically or scientifically certain, but it must be informed by a "sound and reliable" medical or scientific explanation. Boatmon, 941 F.3d at 1359; see also Knudsen, 35 F.3d at 548; Veryzer v. Sec'y of Health & Hum. Servs., 98 Fed. Cl. 214, 257 (2011) (noting that special masters are bound by both § 13(b)(1) and Vaccine Rule 8(b)(1) to consider only evidence that is both "relevant" and "reliable"). If Petitioner relies upon a medical opinion to support her theory, the basis for the opinion and the reliability of that basis must be considered in the determination of how much weight to afford the offered opinion. See Broekelschen v. Sec'y of Health & Hum. Servs., 618 F.3d at 1347 (Fed. Cir. 2010) ("The special master's decision often times is based on the credibility of the experts and the relative persuasiveness of their competing theories."); Perreira v. Sec'y of Health & Hum. Servs., 33 F.3d 1375, 1377 n.6 (Fed. Cir. 1994) (stating that an "expert opinion is no better than the soundness of the reasons supporting it" (citing Fehrs v. United States, 620 F.2d 255, 265 (Ct. Cl. 1980))).

The undersigned finds Petitioner failed to provide preponderant evidence of a sound and reliable theory to explain how the flu vaccine can cause anti-GBM/Goodpasture's syndrome. There are several reasons for this finding.

First, Petitioner's experts did not explain how the flu vaccination can cause anti-GBM/Goodpasture's syndrome. Dr. Goldstein acknowledged that the mechanism of injury to explain how the flu vaccine could cause the illness is unknown. He attributed the lack of knowledge to the rarity of the illness combined with the rare incidence of significant adverse events to flu vaccination. And he argued that "inadequate data" does not prove "there is no causal connection between vaccination and Goodpasture's [s]yndrome." Pet. Ex. 45 at 2. Dr. Goldstein further asserted that "[a]llowance must be made in this case for the possibility of novel biological events." Id.

Inadequate data, even in the face of rare events, however, does not constitute preponderant evidence. And allowances for possibilities is not the legal standard for a finding of entitlement to compensation under the Vaccine Act. Possibilities are not sufficient to establish

causation. See, e.g., Waterman, 123 Fed. Cl. at 573-74; Moberly, 592 F.3d at 1322 (emphasizing that "proof of a 'plausible' or 'possible' causal link between the vaccine and the injury" does not equate to proof of causation by a preponderance of the evidence). Moreover, theories that are speculative and/or conclusory in nature are insufficient.

Dr. Patel's opinion is overly simplistic and vague, and he fails to acknowledge the current knowledge about the complex pathogenesis of the illness. He stated that generally, vasculitic syndromes "are known to be triggered by our immune system. Once the immune complex is formed, it travels via the blood vessels and deposits within them causing them damage." Pet. Ex. 17 at 2.

On the whole, the failure of Petitioner's experts to articulate a mechanism may simply reflect the current state of medical and scientific knowledge—that what causes anti-GBM/Goodpasture's syndrome is not known. Although much is known about the molecular structure of the basement membranes in the kidneys and lungs, as well as the autoantigen expressed in these tissues, the way in which the disease is induced is not understood. See, e.g., Resp Ex. D, Tab 3 at 1 (noting although great progress has been made in understanding its pathogenesis, the etiology of the illness remains unknown); Pet. Ex. 38 at 1-2 (acknowledging triggers that initiate responses causing anti-GBM disease are not well understood); Pet. Ex. 22 at 8 ("[T]he inciting events that cause autoimmunity to GBM antigens remain unclear.").

Petitioner need not make a specific type of evidentiary showing to prove that a theory is sound and reliable by preponderant evidence. Given the state of current scientific knowledge, there is no way that a petitioner could satisfy such a requirement. See Knudsen, 35 F.3d at 549 (explaining that "to require identification and proof of specific biological mechanisms would be inconsistent with the purpose and nature of the vaccine compensation program"). However, the evidence shows that how anti-GBM disease is induced is not known. And Petitioner did not provide preponderant evidence to show that the flu vaccine can induce kidney or lung injury so as to cause anti-GBM/Goodpasture's syndrome.

Second, the medical literature and Respondent's experts effectively established that theories relevant to other types of vasculitis cannot be extended to the illness here without taking into account the molecular basis of the disease and whether it is similar to what is known about anti-GBM/Goodpasture's syndrome. For example, Petitioner referred to Patel and Shah about cases of renal complications reported after vaccination, including after flu vaccination. But none of the reported cases involved anti-GBM disease after the flu vaccination. And other vascular diseases can be distinguished from Goodpasture's syndrome based on what is known about its pathogenesis. Dr. Jarad described the Collagen IV family of molecules that form the mesh-like structures in the basement membrane in anti-GBM disease. The most common antibody is thought to target the NC1 of the Collagen IV α3 chain and the Collagen IV α5 chain. He also explained these structures may be "immune privileged." Resp. Ex. B at 8. Due to the complexity of the tightly bonded structures and their immune protection, the links between Collagen IV molecules must be broken, the immune system triggered (B and T lymphocytes must be stimulated), and autoantibodies produced. Moreover, in some patients, the anti-GBM antibody can be detected years before disease manifestation. Therefore, generalizations about causal mechanisms applicable to other vascular diseases with different molecular makeup and

underlying pathology cannot be imputed to Goodpasture's syndrome.

More specifically, Petitioner's use of case studies or other medical literature involving patients with ANCA associated vasculitis are not persuasive evidence of causation because that condition involves different antibodies than the condition here. For example, Dr. Goldstein cited the Norton et al. case of double seropositive (ANCA and anti-GBM) vasculitis that occurred after receipt of a flu vaccine. Petitioner also cited the Jeffs et al. case report of a patient who developed ANCA-associated vasculitis following a flu vaccine. Without evidence that the underlying causal mechanisms of the two different conditions are the same, mechanisms applicable to an ANCA positive disease cannot be imputed to anti-GBM disease.

Third, Petitioner's experts also invoked infectious etiologies presumably to bolster their argument that a vaccine preventing the same infection can trigger an autoimmune illness. But that argument is not persuasive when the evidence and the literature does not show that such infections are causally associated with the condition. There are two reasons that the infectious argument is unavailing. First, Respondent's experts distinguished the flu infection from the flu vaccination as a trigger for anti-GBM/Goodpasture's syndrome because they explain that the flu infection causes damage to the lung, exposing cryptic epitopes—targets for disease causation. There is no evidence that the flu vaccination can cause lung injury like a flu infection, and Dr. Goldstein agreed this position was reasonable. The second reason that the infectious model is not persuasive here is the lack of support in the medical literature. While the original case of Goodpasture's syndrome was evaluated in association with flu infection, more recent medical literature explained that the case originally described by Dr. Goodpasture "likely had [ANCA] antibody disease rather than true Goodpasture's." Pet. Ex. 39 at 5; see Resp. Ex. D, Tab 2 at 1. And although Wilson and Smith suggested theories for how flu infection could play a causal role in anti-GBM illness, they opined the association between their patient's prior flu infection and her anti-GBM illness "may have been coincidental." Pet. Ex. 26 at 3; see also Pet. Ex. 22 at 2 (noting associations between anti-GBM disease and infections are speculative and not proven).

The fourth problem with Dr. Goldstein's and Dr. Patel's opinions is that they are conclusory. Dr. Goldstein opined it is "reasonable and probable to conclude that the induction of Goodpasture's disease, an autoimmune phenomenon, is consequent to and the result of [flu] vaccination in this case." Pet. Ex. 16 at 2. Dr. Patel's opinion is similarly conclusory. He stated that generally, vasculitic syndromes "are known to be triggered by our immune system. Once the immune complex is formed, it travels via the blood vessels and deposits within them causing them damage." Pet. Ex. 17 at 2. This opinion does not begin to consider what is currently known about the pathogenesis of the illness as described in the medical literature. And it does not explain the role of the flu vaccine.

When evaluating whether petitioners have carried their burden of proof, special masters consistently reject "conclusory expert statements that are not themselves backed up with reliable scientific support." Kreizenbeck v. Sec'y of Health & Hum. Servs., No. 08-209V, 2018 WL 3679843, at *31 (Fed. Cl. Spec. Mstr. June 22, 2018), mot. for rev. denied, decision aff'd, 141 Fed. Cl. 138, aff'd, 945 F.3d 1362 (Fed. Cir. 2020). The undersigned will not rely on "opinion evidence that is connected to existing data only by the ipse dixit of the expert." Prokopeas v. Sec'y of Health & Hum. Servs., No. 04-1717V, 2019 WL 2509626, at *19 (Fed. Cl. Spec. Mstr.

May 24, 2019) (quoting Moberly, 592 F.3d at 1315). Instead, special masters are expected to carefully scrutinize the reliability of each expert report submitted. See id.

The fifth reason that the undersigned finds that Petitioner has not met her burden of proof is due to the lack of evidence that the flu vaccine can cause anti-GBM/Goodpasture's syndrome. In the medical literature filed herein, there is only one case report of anti-GBM disease following the flu vaccination. See Pet. Ex. 25 at 2 tbl.1, 5 (anti-GBM disease reported after pneumococcal vaccine). While the undersigned generally finds case studies may provide some evidence of causation, a single case report is not sufficient, without more, to constitute sufficient evidence upon which to conclude that the flu vaccination can cause anti-GBM/Goodpasture's syndrome, especially in light of the other deficiencies discussed above. The other case reports either do not involve the same disease or do not involve the flu vaccination. Therefore, the relevance of these case reports is not clear. Case reports about one vaccine cannot automatically be imputed to a different vaccine, particularly when the mechanism offered has not been suggested as to the vaccine at issue. The same is true for different diseases. "An expert may 'extrapolate from existing data,' and use 'circumstantial evidence,' [b]ut the reasons for the extrapolation should be transparent and persuasive." K.O. v. Sec'y of Health & Hum. Servs., No. 13-472V, 2016 WL 7634491, at *12 (Fed. Cl. Spec. Mstr. July 7, 2016) (internal citations omitted) (first quoting Snyder v. Sec'y of Health & Hum. Servs., 88 Fed. Cl. 706, 743 (2009); and then quoting Althen, 418 F.3d at 1280).

Here, Petitioner's experts did not offer any persuasive reasons for extrapolating from the other vaccines to the flu vaccine. See K.O., 2016 WL 7634491, at *12 (finding the case reports offered by Petitioner as having even less value than case reports do generally because they reported a sequence in which a vaccine, but not the vaccine at issue, preceded the onset of the injury at issue (citing Campbell v. Sec'y of Health & Hum. Servs., 97 Fed. Cl. 650, 668 (2011))); Crosby v. Sec'y of Health & Hum. Servs., No. 18-1478V, 2021 WL 3464125, at *9 (Fed. Cl. Spec. Mstr. July 22, 2021) (declining to give substantial weight to an article because it was on a different vaccine than the one at issue making reasoning difficult); see also Deshler v. Sec'y of Health & Hum. Servs., No. 16-1070V, 2020 WL 4593162, at *19-21 (Fed. Cl. Spec. Mstr. July 1, 2020) (declining to attribute case reports on the flu vaccine to pneumococcal vaccines); McDonald v. Sec'y of Health & Hum. Servs., No. 15-612V, 2023 WL 2387844, at *23 (Fed. Cl. Spec. Mstr. Mar. 7, 2023).

Finally, there does not appear to be any other Vaccine Program case involving anti-GBM/Goodpasture's syndrome where a ruling, dismissal, or decision based on stipulation has

been filed.[67] The lack of other cases shows the rarity of the condition but also illustrates that anti-GBM/Goodpasture's syndrome has not been associated with the flu vaccine in the Program.

In summary, for all the reasons described, Petitioner has failed to offer a sound and reliable medical theory in support of his claim. Thus, the undersigned finds Petitioner has failed to provide preponderant evidence with respect to the first Althen prong.

B. Althen Prong Two

Under Althen prong two, Petitioner must prove by a preponderance of the evidence that there is a "logical sequence of cause and effect showing that the vaccination was the reason for the injury." Capizzano, 440 F.3d at 1324 (quoting Althen, 418 F.3d at 1278). "Petitioner must show that the vaccine was the 'but for' cause of the harm . . . or in other words, that the vaccine was the 'reason for the injury.'" Pafford, 451 F.3d at 1356 (internal citations omitted).

In evaluating whether this prong is satisfied, the opinions and views of the vaccinee's treating physicians are entitled to some weight. Andreu, 569 F.3d at 1367; Capizzano, 440 F.3d at 1326 ("[M]edical records and medical opinion testimony are favored in vaccine cases, as treating physicians are likely to be in the best position to determine whether a 'logical sequence of cause and effect show[s] that the vaccination was the reason for the injury.'" (quoting Althen, 418 F.3d at 1280)). Medical records are generally viewed as trustworthy evidence since they are created contemporaneously with the treatment of the vaccinee. Cucuras, 993 F.2d at 1528. While the medical records and opinions of treating physicians must be considered, they are not binding on the special master. § 13(b)(1)(B) (specifically stating that the "diagnosis, conclusion, judgment, test result, report, or summary shall not be binding on the special master or court"); Snyder, 88 Fed. Cl. at 746 n.67. "As with expert testimony offered to establish a theory of causation, the opinions or diagnoses of treating physicians are only as trustworthy as the reasonableness of their suppositions or bases." Welch v. Sec'y of Health & Hum. Servs., No. 18-494V, 2019 WL 3494360, at *8 (Fed. Cl. Spec. Mstr. July 2, 2019).

Since Petitioner failed to prove Althen prong one, it follows that she cannot prove Althen prong two. However, even if Petitioner had proven Althen prong one, the undersigned finds Petitioner has failed to show by preponderant evidence that there is a logical sequence of cause and effect showing Petitioner's flu vaccine caused her anti-GBM/Goodpasture's syndrome.

[67] There are three cases involving nephritis or nephrotic syndromes, but those conditions are different than anti-GBM/Goodpasture's syndrome. See Stewart v. Sec'y of Health & Hum. Servs., No. 03-1877V, 2005 WL 419692, at *1 (Fed. Cl. Spec. Mstr. Jan. 28, 2005) (minimal change disease); Miles v. Sec'y of Health & Hum. Servs., No. 12-254V, 2018 WL 3990987, at *36 (Fed. Cl. Spec. Mstr. June 28, 2018) (pre-existing nephrotic syndrome); Isaacson v. Sec'y of Health & Hum. Servs., No. 14-1056V, 2020 WL 7586971, at *11 (Fed. Cl. Nov. Spec. Mstr. 25, 2020) (RPGN/progressive glomerulonephritis with monoclonal IgG deposits). But see Larive v. Sec'y of Health & Hum. Servs., No. 99-429V, 2004 WL 1212142, at *12 (Fed. Cl. Spec. Mstr. May 12, 2004) (focal segmental glomerulosclerosis form of nephrotic syndrome).

First, Petitioner tested negative for ANCA antibodies and did not have ANCA-associated vasculitis like some of the patients in the medical literature cited by Petitioner's experts. As described above relevant to Althen prong one, ANCA-associated vasculitis has been reported after the flu vaccine. However, Petitioner did not have ANCA antibodies. Thus, the mechanism that causes that disease cannot be presumed as causal here.

Additionally, the undersigned finds that while some of Petitioner's treating physicians documented her report of symptoms and/or their temporal association with vaccination, they did not opine that her flu vaccine caused her illness.[68] See, e.g., Pet. Ex. 3 at 13, 16 (documenting Petitioner complained of nausea and an episode of vomiting "after getting the flu shot"); Pet. Ex. 5 at 2 (indicating Petitioner reported she "got the flu vaccine [two] weeks ago and . . . had symptoms since then"); Pet. Ex. 6 at 1 (Petitioner "reported getting sick approximately two weeks ago after receiving the flu vaccine.").

After reviewing the medical records, while some records documented that Petitioner reported a temporal association between vaccination and onset of symptoms, the undersigned finds that none of Petitioner's treating physicians opined that her flu vaccination caused her anti-GBM/Goodpasture's syndrome. "A treating physician's recognition of a temporal relationship does not advance the analysis of causation." Isaac v. Sec'y of Health & Hum. Servs., No. 08-601V, 2012 WL 3609993, at *26 (Fed. Cl. Spec. Mstr. July 30, 2012), aff'd 108 Fed. Cl. 743 (2013), aff'd 540 F. App'x 999 (Fed. Cir. 2013); see also A.T. v. Sec'y of Health & Hum. Servs., No. 16-393V, 2021 WL 6495241, at *28 (Fed. Cl. Spec. Mstr. Dec. 17, 2021) (finding that Petitioner's treating physicians "considered, though did not conclude," that Petitioner's vaccine significantly aggravated her condition); Robertson v. Sec'y of Health & Hum. Servs., No. 18-554V, 2022 WL 17484980, at *17 (Fed. Cl. Spec. Mstr. Dec. 7, 2022) (finding treating physicians' statements of mere suspicion fall short of an opinion supporting vaccine causation); Cedillo v. Sec'y of Health & Hum. Servs., 617 F.3d 1328, 1347 (Fed. Cir. 2010) (concluding the special master did not err in affording little weight to the opinions of Petitioner's treating physicians where "none of the treating physicians concluded that the [] vaccine caused [Petitioner's] [condition]").

Accordingly, the undersigned finds that Petitioner failed to satisfy her burden under Althen prong two.

[68] To the extent that any of Petitioner's treating physicians associated her illness with any antecedent events, these included a preceding URI or her use of ibuprofen. See, e.g., Pet. Ex. 5 at 3 ("[I]buprofen [was a] possible cause."); Pet. Ex. 5 at 76 (noting Petitioner used NSAIDs recently "which [was] a possibility"); Pet. Ex. 6 at 1 (Risk assessment included use of "[i]buprofen in the last [two] weeks."); Pet. Ex. 7 at 16 (noting Petitioner "had URI with hematuria in mid-October"). However, the experts did not opine that Petitioner's URI or use of ibuprofen more likely than not caused her illness, and therefore, the undersigned does not address either of these events as an alternate cause.

C. Althen Prong Three

Althen prong three requires Petitioner to establish a "proximate temporal relationship" between the vaccination and the injury alleged. Althen, 418 F.3d at 1281. That phrase has been defined as a "medically acceptable temporal relationship." Id. A petitioner must offer "preponderant proof that the onset of symptoms occurred within a timeframe for which, given the medical understanding of the disorder's etiology, it is medically acceptable to infer causation-in-fact." de Bazan, 539 F.3d at 1352. The explanation for what is a medically acceptable time frame must also be consistent with the theory of how the relevant vaccine can cause the injury alleged (under Althen prong one). Id.; Koehn v. Sec'y of Health & Hum. Servs., 773 F.3d 1579, 1243 (Fed. Cir. 2014); Shapiro, 101 Fed. Cl. at 542; see also Pafford, 451 F.3d at 1358. Thus, prong three contains two parts. First, Petitioner must establish the "timeframe for which it is medically acceptable to infer causation" and second, Petitioner must demonstrate that the onset of the disease occurred in this period. Shapiro, 101 Fed. Cl. at 542-43.

Petitioner received her flu vaccination on October 11, 2016. She first presented for care on October 21, 2016, complaining of an episode of vomiting and decreased appetite that began two weeks prior, after getting the flu shot. On the same day, Petitioner went to the ED reporting "she got the flu shot [two] weeks ago and . . . had [symptoms] since then." Pet. Ex. 5 at 2. Review of systems was positive for sweating, nausea, constipation, decreased appetite, and headache. On October 25, 2016, Petitioner saw nephrologist Dr. Voinescu and "reported getting sick approximately two weeks ago after receiving the flu vaccine with symptoms of headache, muscle aches, cough, fatigue[,] and night sweats." Pet. Ex. 6 at 1. She repeated this same history during her subsequent admissions and when giving histories to new healthcare providers. When she saw Dr. DeSilva, the nephrologist in Pittsburgh, on March 16, 2017 for a second opinion, Petitioner reported that she received a flu vaccine on October 11, 2016, and "within 24 h[ours] felt myalgias/chills/night sweats." Pet. Ex. 12 at 483.

Based on this clinical course, Dr. Goldstein opined that the onset of Petitioner's symptoms was 24 hours after vaccination. Dr. Patel did not offer an opinion as to onset of Petitioner's illness, only the first date that Petitioner presented for care. Both relied on the Watanabe review article which stated that the median duration from vaccination to onset of vasculitis was 12 days. And Dr. Patel opined that it usually takes seven to 10 days to develop an antibody response, although he explained this can occur "shortly outside" of this time frame. Pet. Ex. 17 at 2. Neither of Petitioner's experts effectively addressed Respondent's experts' opinions that a 24-hour onset was too soon to implicate the flu vaccine as a cause. Dr. Goldstein offered "the possibility" that Petitioner had "subclinical" disease that "blossomed" into disease due to vaccination, but he does not explain how onset could occur so quickly even given this possibility. Pet. Ex. 45 at 2.

Dr. Jarad and Dr. Levinson agreed that onset occurred the day after vaccination. However, they disagreed that onset was appropriate given what is known about the pathogenesis of anti-GBM/Goodpasture's syndrome. Both opined that a 24-hour onset is too short to induce autoantibodies and T cell reactivity. Citing the IOM, Dr. Jarad noted the latency phase between exposure and response is four to seven days for T cells and 7 to 10 days for B cells. He further explained that given what is known about the pathogenesis of anti-GBM/Goodpasture's

syndrome, it usually takes "weeks, if not months" for autoantibody induction and clinical disease. Resp. Ex. B at 10. Thus, he opined that 24 hours was "not sufficient to disrupt the links between Collagen IV molecules, sensitize B and T lymphocytes, [] generate autoantibody, maintain the disruption of the Collagen IV molecules[,] and continue to expose the cryptic antigen to further attack by the immune system." Id. (emphasis omitted).

The undersigned finds the opinions of Dr. Jarad and Dr. Levinson more persuasive because they are consistent with what is known about the pathogenesis of the illness as described in the medical literature. The undersigned finds that a 24-hour onset is too soon for a vaccine to be the trigger of anti-GBM/Goodpasture's syndrome.

Therefore, the Petitioner has failed to provide preponderant evidence of an appropriate temporal association between her flu vaccination and the onset of her symptoms of anti-GBM/Goodpasture's syndrome.

V. CONCLUSION

Petitioner has suffered a very serious and life-threating illness, eloquently described in the diary submitted and supported by her medical records. The undersigned extends her sympathy for the physical and emotional suffering Petitioner has been through due to her illness. However, the undersigned's Decision cannot be based on her sympathy, but must be based on the evidence and the law.

For the reasons discussed above, the undersigned finds that Petitioner has failed to provide preponderant evidence of causation, and therefore, the Petition must be dismissed.

IT IS SO ORDERED.

s/Nora Beth Dorsey
Nora Beth Dorsey
Special Master